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- Cardiac Surgery in Covid Era—an Experience at Our Tertiary Care Center Short Title - Cardiac Surgery in COVID Pandemic.
- Efficacy and Safety of Percutaneous Transhepatic Biliary Drainage in Malignant Biliary Obstruction—A Single Tertiary Centre Experience.
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- Intramuscular Massetric Hemangioma Resembling Parotid Swelling -A Rare Case Report.



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ORIGINAL ARTICLE

Innovative Way of Teaching Pharmacology through E-posters during Pandemic Times

Monica Jain*, Uma Advani**, Shivankan Kakkar**, Rupa Kapadia*, Arun Singh***, Anil Bhandari***

ABSTRACT

Introduction: The education systems have evolved dramatically in the present times. Most of the people have experienced some form of digital learning in this pandemic. There is still immense potential and lot to explore in approaches to digital design that can make online learning engaging and exciting.

Methodology: When the pandemic happened, we at SMS Medical College Hospital, INDIA started online working and conducting teaching and training classes remotely. Departmental residents were involved first in the e-poster making activity and they submitted the same in various conferences. The second MBBS batch of 2018 (regular and remanded) comprising of 264 students was divided into 18 groups (15 students each in group). Core areas from the subject pharmacology were chosen and allotted to individual groups. An anonymous survey in form of Google forms was taken from students upon completion of the activity. The project activity was graded.

Results: The post activity survey results indicated that e-posters provide a transition from a stationary piece of paper to a more dynamic experience that actively connects and can be used to provide newer insights to learning. There was practically no cost involved.

Conclusion: The ramifications of COVID-19 are going to be with us for a long time and in order not to disadvantage an entire generation there is a need to change entrenched values. It requires out of the box thinking, to be creative and to be able to adapt and evolve.

Keywords: Innovative Way of Teaching, Pandemic, E-posters

INTRODUCTION

The education systems have evolved dramatically in the present times. Most of the people have experienced some form of digital learning in this pandemic. The world is evolving, and so is teaching. The needs and expectations of learners – and the challenges for those who create educational materials have become more diverse and complex. For medical education it had been a challenging task from day one. It can be said that, there is no substitute to regular teaching in medicine because of the range of skills and techniques (including the most important patient communication skills) that are needed to be acquired.¹ This is important since the new competency based medical curriculum is in pipeline to be implemented in all the medical colleges of INDIA. Having said that, the top medical institutes took up this daunting job and developed methods for effective teaching and training remotely.

Here, we discuss our institutional experience of an innovative method using electronic posters (e-posters) for teaching pharmacology to undergraduate medical (MBBS) batch of 2018. The idea was generated while attending the international medical conferences which had to be conducted online this year and wherein e-posters were being encouraged. At first the residents of the department were trained through an e-poster activity and subsequently they framed and submitted the e-posters in leading conferences worldwide. Thereafter the activity was formulated and conducted for the whole undergraduate medical, nursing and paramedical batches. There is still immense potential and lot to explore in

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approaches to digital design that can make online learning engaging and exciting.²

METHODOLOGY

When the pandemic happened, we at SMS Medical College Hospital, INDIA started online working and conducting teaching and training classes remotely. We started using online learning platforms and made them accessible to our medical, nursing and paramedical students but we were not that sure and confident that our learners were getting the best benefits from the sessions they attended online. For this the feedback from the students was taken using google forms and it was found that most of the students were either lacking interest in the online classes or had limited connectivity. The students came from varying backgrounds and from places in INDIA where the access to the internet had not been that easy. They had to learn at their own pace if or when technological resources were made available.

In the meantime, we were continuously trying to discover more ways to make the online platform suitable to our specialized needs. There is a science behind the best

online learning practices³. We explored the various transformative approaches to digital learning, created our own and among them the one that had an encouraging response was that of electronic poster (e-poster) learning.

Our students had no previous experience or training for designing e-posters. We uploaded a 30 minute didactic training video on various techniques for making an effective e-poster activity. The video ensured proper orientation of the students on what was expected out of the activity⁴. This was made available to them on social media sites YouTube and Whatsapp for further access and additional materials. Departmental residents were involved first in the e-poster making activity and they submitted the same in various conferences. The second MBBS batch of 2018 (regular and remanded) comprising of 264 students was divided into 18 groups (15 students each in group). Core areas from the subject pharmacology were chosen and allotted to individual groups. (Table 1). An anonymous survey in form of Google forms was taken from students upon completion of the activity. The project activity was graded.⁵

Table 1: Assignment of e-poster group-wise among the Second MBBS pharmacology students

ROLL NO.s	GROUP CATEGORY	TOPIC OF POSTER
1-15	A	Routes of drug administration 3 posters Enteral, Parenteral and newer
15-30	B	Mechanism of drug action 3 posters G protein coupled receptor Other receptor mediated Non receptor mediated action
31-45	C	Kinetics of elimination 3 poster with graphs and examples First order, Zero order and Mixed orders
46-60	D	TYPE A ADR TYPE B ADR PHARMACOVIGILANCE
61-75	E	Biotransformation of drugs phase 1 and phase 2 two posters 3rd poster of Enzyme induction and Inhibition
75-90	F	Pharmacotherapy of glaucoma, myasthenia gravis, organophosphorus poisoning 3 posters
91-105	G	Adrenergic receptors and drug classification one poster, Beta blockers classification and uses 2nd poster, Alpha blockers classification and uses third poster
106-120	H	Diuretics 3 posters covering three major groups with uses and mechanism and site of action

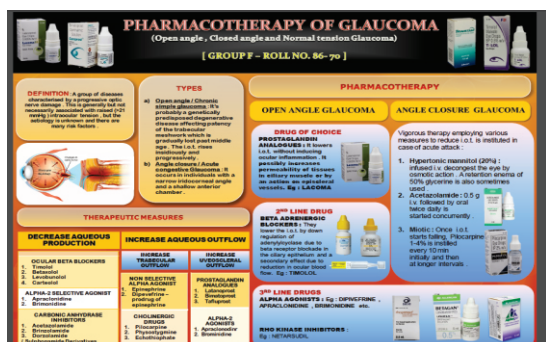
ROLL NOS	GROUP CATEGORY	TOPIC OF POSTER
121-135	I	Drug therapy of angina pectoris one poster with details of nitrates, MI second poster Calcium channel blockers mechanism of action and classification uses one poster.
136-150	J	Drugs for cardiac arrhythmia three posters covering major drugs
151-165	K	Drug for dyslipidemia one poster for lipid disorder and types of lipoprotein, second classification of drugs third poster details of each group
165-180	L	NSAIDs classification with mechanism and uses, Pharmacotherapy of rheumatoid arthritis Pharmacotherapy of gout one poster
181-195	M	Prokinetic drugs classification, mechanism of action and adverse effects.
195-210	N	Drug treatment of peptic ulcer with classification, H2 blockers, pump blockers three posters
211-225	O	Antitubercular drugs, classification, mechanism of action and side effect of first line category wise treatment of TB and treatment of multidrug resistance and extensively resistance tuberculosis.
226-240	P	Drugs treating HIV, highly active antiretroviral drugs and treatment protocol
241-255	Q	Antiepileptic drugs, classification, mechanism of action & Recent drugs
256-264	R	Drug treatment of type 2 diabetes mellitus three posters

RESULTS

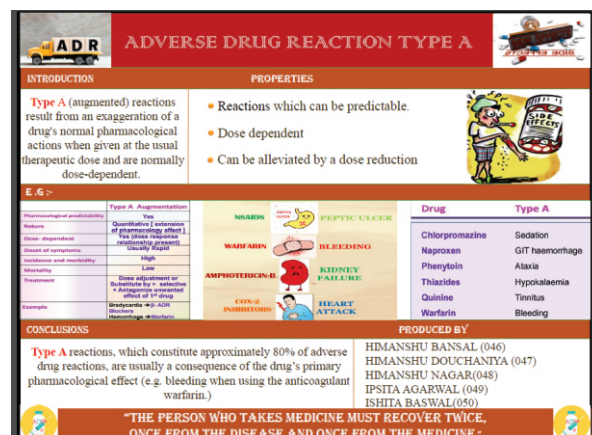
The whole IInd MBBS batch of 2018 submitted a total of 50 e-posters on the allotted core topic areas. The evaluation of the e-posters was done on the basis of design, quality of content, structuring, creativity and e-presentation. Upon grading individual e-posters- 3 best projects were awarded with online certification. E-poster booklet was prepared and kept in the library for future reference and further improvement. A sample copy of the e-posters submitted by our students is given here. (Figure 1).

Figure 1: Sample e-posters submitted by students A & B

a)



b)



The activity ensured that the students participated in groups, developed team spirit, an in depth knowledge of the topic that was allotted (even when the internet connectivity was poor) and generated curiosity in the young minds. It also gave them a chance to be creative, versatile, participate in the conferences and developed their patient communication skills. E-posters are still comparatively new and a short coming in a few e-posters

was that students simply created copy-paste e-versions of basic google slides. There is a need for additional computation skills to be taught to the medical students.⁶

The post activity survey results indicated that e-posters provide a transition from a stationary piece of paper to a more dynamic experience that actively connects and can be used to provide newer insights to learning. There was practically no cost involved.

CONCLUSION

It is possible to teach medical, nursing and paramedical students the basics of e-poster design, and further expand their creative and communication skills into the domain of e-communications. The outlined innovative method can prepare the students as e-poster creators for academic conferences, patient communication and especially for quality learning.

The ramifications of COVID-19 are going to be with us for a long time and in order not to disadvantage an entire generation there is a need to change entrenched values. It requires out of the box thinking, to be creative and to be able to adapt and evolve.

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ORIGINAL ARTICLE

Cardiac Surgery in Covid Era—an Experience at Our Tertiary Care Center Short Title - Cardiac Surgery in COVID Pandemic

Hemlata Verma*, Anula Sisodia*, RM Mathur**, Anil Sharma**, R. K. Yadav**, Sanjeev Devegadha**

ABSTRACT

Background: A sudden emergence of global pandemic due to SARS- Cov -2 has changed the scenario of management of non COVID diseases. With very high infectivity rate and stormy course, this disease has made the lives of people miserable so with the health care facilities and treatment. All the medical fraternities are in the state of confusion that how to treat or not to treat the patients of illness other than the corona virus infection.

We are sharing our experience of cardiac surgery at our tertiary center in lockdown and unlockdown period.

Material and Method: This is a retrospective study from April 2020 to November 2020. We have operated upon 232 cases in this duration.

Results: Out of 232 cases – Overall mortality –26 Post covid operated –4

Number of covid positive after surgery – 3 Post covid Mortality –1

Conclusion: Use of N95 mask, PPE kit or HIV KIT, with regular sanitization of hands have made possible to perform cardiac surgery in this difficult situation on the patients of cardiac illness which usually cannot wait longer.

Key Words: Pandemic, SARS-Cov 2, Cardiac Illness, N95 mask, PPE KIT, HIV KIT, sanitization.

INTRODUCTION

This year 2020 came to our life with challenge of facing global pandemic of SARS-Cov 2 infection. A simple flu- like respiratory infection changes its behavior within few days and becomes a systemic infection causing various symptoms and signs related to lungs,

heart, gastrointestinal tract, nervous system, musculoskeletal system and eye. Although, mortality rate is not very high and infection is curable with available drugs but once it involves lungs or becomes systemic with cytokine storm then there are very high chances of mortality.

Because of very high rate of infection, through aerosols, air droplets, fomite and surface transmission, and uncertainty of clinical outcome of the infection Government of INDIA decided to contain the infection by imposing lockdown.

The Government tried to improve the health care facilities during lockdown by making availability of more medicines, ICU beds, general wards, oxygen, ventilators and other equipments for the coming challenges in future.

But as number of SARS-Cov 2 infected cases increased, our tertiary health care hospital, which is largest government hospital in the western region, was converted into free covid care hospital to provide treatment of all corona virus infected cases. OPDs and all operation theatres were closed for routine surgeries except for emergency procedures. ICUs, all nursing staff, and doctors were posted for care of SARS-Cov 2 infected patients.

But continuing to defer all elective surgeries may lead to a situation where a lot of patients may die of their original condition.

We started routine cardiac surgery once lockdown was relaxed and other government associated hospitals took over the charge of management of covid 19 infected cases making our center available for management of all other diseases.

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With increasing covid cases, question of protecting all health care workers persists, and in such circumstances, it is better if we can formulate broad guidelines for us.

With the available knowledge about corona virus and protection protocols, we started doing routine cardiac cases.

So, we are sharing our experience of last eight months of performing open heart surgery with minimum resources available and with due protection of all health care workers from getting the corona virus infection.

MATERIALS AND METHOD

This is a retrospective study of 232 cases of open heart surgery operated at our center during 8 months from April 2020 to November 2020. Knowing the highly contagious nature of the SARS Corona-2 virus, we established our protocol to decrease the exposure of all doctors, nurses, floor workers, as well as patients.

We reduced the number of cases operated per theatre to one case per table followed by complete sterilization of OT premises daily. As we know that operating on a suspected covid patient was associated with very high chances of infection to all health care workers we developed our protocol to limit the spread of infection. We started to follow the guidelines mentioned below—

1. A separate ward was established to admit the patients before detection of corona infection.
2. The patients were subjected to two covid RT PCR test 72 hours apart and HRCT thorax in all patients regardless of symptoms present or not.
3. Once, a single report comes negative for covid infection, they were shifted to preoperative surgical ward. Any patient, who comes positive, was shifted to covid isolation hospital for further management.
4. RTPCR test was repeated every 72 hourly till the date of surgery.
5. Distance between two beds was kept according to the two meter distance criteria.
6. All the patients, relatives, and health care workers were asked to strictly follow the face mask application guidelines with properly covering the nose and mouth all the time.
7. Only one or two, and the same attendants, who were

covid negative, were allowed to stay with the patient till the time of discharge.

8. Patients were taken for surgery once their report is negative for covid infection day before or the morning of surgery.
9. Patient's face mask was removed only just before endotracheal intubation.
10. PPE kit with face shield and N95 mask were put on by anesthetist, nursing staff, and floor workers. Only, minimum required number of health care workers was allowed to stay inside the OT.
11. Surgeons wore PPE kit or HIV kit with N95 mask covered with another surgical mask and Loop.
12. During sternotomy, the sterna saw was kept covered with wet sponge.
13. Minimum utilization of cautery or use of smoke free cautery.
14. Early extubation in ICU and early discharge.
15. Testing for covid-19 infection in postoperative period and if patient comes positive, then shifted to covid care hospital.
16. Any patient planned for surgery and comes positive after initial negative report, were shifted to covid care hospital and operated after one and half month of becoming covid negative.

RESULTS

Total 232 patients were operated in eight months of corona era from April 2020 to November 2020 in cardiac surgery department of SMS Hospital Jaipur, Rajasthan.

Only 2 cases were operated in LOCKDOWN period of April and May 2020 with one case in each month, one was critical left main disease with ongoing severe angina and other was LA myxoma with pulmonary edema.

Once Lockdown was relaxed our services were resumed to a limited extent. All type of cardiac cases including simple congenital cardiac surgery in pediatric cases were operated.

Out of 232 cases, 92 were female (39.65%) and 140 were male patients (60.34%).

Maximum cases were in age group of 31 – 70 years (153 cases, 65.94%) . 8 cases were more than 70 years of age (3.44%) and 20 cases were in pediatric age group ranging from 2 month of age to 10 years (8.62%).

Valve replacement was the commonest surgery with 96 cases (41.37%) followed by Coronary artery bypass grafting (CABG) with 84 out of 232 cases (36.20%).

In congenital cases, central shunt (1), ASD closure (15), VSD closure (8), AVCD (1), TOF repair (8), and TAPVC repair (3) were the main procedure.

Difficult cases were also operated including DVR with BENTALL procedure (1), CABG with Aortobifemoral bypass grafting (1), CABG with MVR (2), Aortic Aneurysm (1), and Redo DVR (1). 2 cases were of LA Myxoma and one case of RA mass.

Other cases operated were tricuspid repair in Ebstein's anomaly and VSD closure with AVR in RSOV.

Overall Mortality rate was 11.20% (26 out of 232).

4 patients who were covid positive in preoperative period, treated first for covid infection and then operated with good postoperative outcome. In these cases 2 were MVR, 1 was sinus venosus ASD, and one was CABG.

3 patients became covid positive in postoperative period. They were shifted to covid care hospital for the management. Out of 3, 2 patients (VSD closure, CABG) were discharged and one patient died due to covid – 19 pneumonia (ASD closure).

The patient who died of covid – 19 pneumonia was RTPCR negative 3 times for covid infection but her CORAD score was 3 on HRCT thorax. In view of being asymptomatic with good oxygen saturation we took her for surgery but the very next day her RTPCR report came positive and her chest x ray was also showing changes related to covid infection. She was on ventilator and treated for corona virus infection but ultimately she succumbed to the infection.

Overall mortality for corona operated patient was 14.28%.

DISCUSSION

The appearance of global pandemic caused by SARS – Covid – 2 or Covid – 19 virus has dramatically affected cardiac surgery worldwide¹.

Many cardiac surgery centers were converted to covid – 19 care units², while our whole hospital, which is the largest government hospital of our state, was converted to covid center resulting in significant

reduction in all types of surgeries related with different surgical branches. Our CTVS department which was operating more than 1100 cases per year before the Corona era has come down to 232 cases of open heart surgery only. Same status was also noted by Fudula DP et al in their study³ with potential negative impact to the community.

By continuing to defer all elective surgeries, a situation will appear where a lot of patients may die of their original condition. So, departments have tentatively restarted their work once lockdown was relaxed. With increasing covid cases the question still persists about the safety of health care workers. In such circumstances, it is better if we can formulate a broad guideline for us.

There are no firm recommendations available to guide decision making for patients requiring cardiac surgery during this pandemic⁴. Although surgical associations have offered guidelines and recommendations on how to conserve resources and triage patients who need more urgent care⁵ but only limited recommendations are available for cardiac surgery⁶⁻⁸.

Operating on a patient who may be corona positive, is putting the life of all health care workers at risk. But for serious patients, like critical CAD, LMSD, severe angina, valvular heart disease in heart failure, surgery is the only treatment.

Looking into the seriousness of this infection efforts were done to decrease the exposure of surgical patients and health care workers to COVID-19, shifting of the required staff to the emergency department and ICU, rationing of the use of critical supplies, including ventilators, PPE Kit, masks, and blood products along with postponement of all elective surgical cases and procedures throughout the United State by Department of Health and Human Services and the American College of Surgeons⁹. We have done various types of simple and complex cardiac cases during this era as we were doing before also but with some more precautions.

The highest risk procedures are (AGPs), which are at higher risk of droplet dispersion and transmission. These AGPs include - intubation, extubation, tracheostomy, bronchoscopy, endoscopy, laparoscopy, any cardiac or thoracic surgery, intercostal chest tube placement, and bovine cautery use¹⁰.

All the above mentioned procedures were done with PPE kit, N95 mask, and face shield on with universal precautions and no health care workers got infected during these procedures.

The use of a N95 respirator or powered air purifying respirator, eye protection, gloves, and gowns are recommended for these procedures in COVID – 19 suspected or positive patients¹⁰⁻¹² but we took all our patients as covid suspected and followed the same precautions as for covid infected cases.

Although there were case reports suggesting transmission of SARS covid – 19 virus to health care workers even when N95 masks were used properly¹³.

Restriction of personnel in OT to only those critical to patient care eg, during anesthesia – only anesthetist and floor workers were allowed. This strategy also helped in reduction of exposure of the health care workers.

Most modern Operation theaters are positive pressure flow type and achieve at best 15 air changes per hour, which would take 18 minutes for 99% removal and 28 minutes for 99.9% removal¹⁴.

This facility is not available at our center so we opted for traditional method i.e, with laminar flow AC on we kept OT doors open, but the main OT corridor gate was closed, so it will allow air to move outside continuously thereby removing air droplets generated during intubation or cautery use during surgery.

The American College of Surgeons has a comprehensive statement on the perioperative use of PPE for patients with or without covid – 19¹².

Although PPE kit was used by anesthetist and other health care workers but for cardiac surgeons it was difficult to operate with PPE kit on because the magnifying loop cannot be used properly without which cardiac surgery is not possible as well as these are long duration surgeries which make surgeons uncomfortable if they wore PPE kit. Therefore, we used HIV kits, N95 mask with surgical mask, and magnifying loop with glasses to protect ourself.

We have also learned from the one mortality that even if RTPCR test is negative the HRCT thorax is more sensitive for detecting covid – 19 infection and if it shows slightest changes we should take it as corona positive.

Table 1: Gender Distribution

S. No.	Gender	Number	Percentage
1	Male	140	60.34%
2	Female	92	39.65%
Total		232	100%

Table 2: Age distribution

S. No.	Age group (years)	Number	Percentage
1	0 – 1	6	2.58%
2	1 – 5	7	3.01%
3	6 – 10	7	3.01%
4	11 – 20	22	9.48%
5	21 – 30	29	12.50%
6	31 – 40	35	15.08%
7	41 – 50	35	15.08%

S. No.	Age group (years)	Number	Percentage
8	51 – 60	44	18.96%
9	61 – 70	39	16.81%
10	71 – 80	8	3.44%
11	>81	0	0%
Total		232	100%

Table 3: Surgical Procedures

S.No.	Surgical procedure	Number	Percentage
1	CABG	84	36.20
2	MVR	49	21.12
3	AVR	20	8.62
4	DVR	27	11.63
5	CABG + Aortobifemoral bypass grafting	1	0.43
6	CABG + MVR	2	0.86
7	DVR + BENTALL Operation	1	0.43
8	ASD closure	15	6.46
9	VSD closure	8	3.44
10	ASD + VSD closure	3	1.29
11	AVCD repair	1	0.43
12	TOF repair	8	3.44
13	Rerouting of TAPVC	3	1.29
14	Ebstein,s anomaly repair	1	0.43
15	LA Myxoma excision	2	0.86
16	RA mass excision	1	0.43
17	Tricuspid regurgitation repair	1	0.43
18	Redo DVR	1	0.43
19	Central shunt	1	0.43
20	Aortic valve repair	1	0.43
21	VSD closure + AVR in RSOV	1	0.43
22	Aortic aneurysm	1	0.43
Total		232	100

Table 4: Overall mortality

S. No.	Surgical procedure	Number of mortality	Percentage
1	MVR	2	
2	AVR	2	
3	DVR	1	
4	CABG	9	
5	DVR + BENTALL	1	
6	Aortic Aneurysm	2	
7	ASD	3	
8	VSD	3	
9	TOF	1	
10	TAPVC	2	
Total		26	

Table 5: Preoperative covid positive operated after being negative –

S.No.	Surgical procedure	Number
1	MVR	2
2	CABG	1
3	ASD closure	1
Total		4

Table 6: Patient becoming covid positive in postoperative period

S.No.	Surgical procedure	Number	Result
1	CABG	1	Discharged
2	VSD Closure	1	Discharged
3	ASD Closure	1	Mortality
Total		3	

CONCLUSION

This newly faced challenge of Covid-19 infection has put all the gears down not in medical field but in every field. With the scarcity of knowledge about this infection and how to operate in this era, we could able to manage with our own developed guidelines in terms of operating the patients as well as protecting lives of all health care workers.

N95 mask, frequent sanitization of hand, and regular sterilization of OT and ICU helped in decreasing the rate of infection.

Initially, it appeared impossible but now it is possible.

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ABBREVIATIONS

SARS – Cov 2	-	severe acute respiratory syndrome corona virus 2
Covid – 19	-	corona virus disease 2019
PPE kit	-	personal protection equipment kit
HIV kit	-	human immunodeficiency virus kit
ICU	-	intensive care unit
OPD	-	Out patient day
OT	-	Operation theatre
RTPCR	-	Reverse transcription polymerase chain reaction
HRCT	-	High resolution computerized tomography
LA	-	Left atrium
RA	-	Right atrium
CABG	-	Coronary artery bypass grafting
ASD	-	Atrial septal defect
VSD	-	Ventricular septal defect
AVCD	-	Atrioventricular canal defect
TOF	-	Tetrology of Fallot
TAPVC	-	Total anomalous pulmonary venous connection
MVR	-	Mitral valve replacement
DVR	-	Double valve replacement
RSOV	-	Ruptured sinus of valsalva
CO-RAD	-	Corona virus 2019 Reporting and Data System
CTVS	-	Cardiothoracic and vascular surgery
CAD	-	Coronary artery disease
LMSD	-	Left main stem disease
AGP	-	Aerosol generating procedure
AC	-	Air conditioner

Efficacy and Safety of Percutaneous Transhepatic Biliary Drainage in Malignant Biliary Obstruction – A Single Tertiary Centre Experience

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ABSTRACT

Background and Aim of the study:

Percutaneous Transhepatic Biliary Drainage (PTBD) is performed as a preoperative procedure for resectable malignancies, prior to neo adjuvant chemotherapy or as a palliative technique. This prospective study was done to evaluate technical success, clinical success, stent/catheter patency rate, survival rate and complications of PTBD in patients with malignant obstructive jaundice.

Materials and method: All patients from June 2018 to November 2019, with malignant obstructive jaundice who have undergone PTBD were included in this study.

Results: One Hundred and One patients were planned for PTBD, technical success was achieved in 93 (92.07%) patients. 97 (96%) patients underwent PTBD for palliation and 4 (4%) for preoperative drainage. Unilateral approach was used in majority of our patients (97.8%). 3 patients (2.9%) underwent internalization with 7 Fr plastic stent. 55 patients were female (54.45%). Mean age was 55.35 ± 22 years. Cause for malignant biliary obstruction was carcinoma gall bladder (77.7%), cholangio carcinoma (9.9%), carcinoma head of pancreas (6.9%), periampullary (3.9%), and metastatic lymphadenopathy at porta (3.2%). Type of block was hilar in 90 patients (89.1%) and lower end block in 11 patients (10.89%). Endoscopic Retrograde Cholangiopancreatography (ERCP) failure was in 25 patients (24.75%). Clinical success was achieved in 88

patients (94.6%). The difference in the pre and post intervention bilirubin levels at 1 month as estimated with wilcoxon signed rank test is found to be statistically significant. Successful biliary drainage had a positive impact on Quality of Life (QOL). Stent/catheter patency period in our study was 51 ± 46 days (range 14 -120 days). Survival in our patients was 74 ± 90 days (Range 15- 270 days).Kaplan-Meier log rank survival analysis showed that there was no statistical significance between the survival rates of the patients when they were grouped according to the post PTBD bilirubin levels.16.1% of our patients had minor complications. Major complications in our centre were 45.15%.

Conclusion: Percutaneous management of malignant biliary obstruction is a good method for palliation with good technical success (92%) and clinical success (94.6%). Unilateral approach was used in majority of our patients (97.8%) as drainage of 25%-30% of normal liver is adequate to improve jaundice and liver functions. PTBD is an effective alternative in ERCP failure patients (25% in our study). Successful biliary drainage alleviates jaundice, improves liver function, and has a positive impact on QOL.

INTRODUCTION

Biliary obstruction is caused by many conditions, including benign and malignant diseases. Malignant biliary obstruction (MBO) is usually caused by gall bladder, cholangiocarcinoma and pancreatic malignancies, metastatic lymphadenopathy and infrequently by hepatic and advanced gastric and

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duodenal malignancies. Frequently the tumors are unresectable at diagnosis and only palliative treatment is possible to improve patients' quality of life¹. The key purpose of biliary interventions in these patients is to decompress the obstructed biliary system and if possible to develop a communication between the biliary tree and the bowel allowing physiological bile flow. This decreases pain, jaundice and occurrence of cholangitis by relieving the obstruction. As hepatic dysfunction is a risk factor for major hepatic resection, biliary drainage helps in improving the liver function prior to surgery or neoadjuvant chemotherapy^{2,3}. For a long time, the relief of obstructive jaundice was accomplished with surgical bilioenteric bypass^{4,5}. However, percutaneous transhepatic biliary drainage (PTBD) or endoscopic drainage are less invasive alternatives and has been used for several decades. Endoscopic stents in the common bile duct is today the first choice to alleviate symptoms and prolong life by decreasing hyperbilirubinemia before surgery, chemotherapy, or as palliation⁶. However, when endoscopic stenting fails in palliative patients, one option is to recommend PTBD and another is to offer best supportive care.

Drainage of 25%-30% of normal liver is adequate to improve jaundice and liver functions^{7,8}. Nevertheless, as bile stasis in any dilated biliary segment can result in infection, drainage of such segments is necessary. Baseline imaging is important to evaluate the extent and severity of biliary dilatation and level of obstruction. Any dilated biliary tree which gets opacified on preliminary cholangiogram needs separate drainage if the communication is narrow, as there is very high incidence of post intervention cholangitis^{9,10}. Hence, cholangiogram should be carefully done in cases hilar obstruction of unilateral drainage to prevent infection¹¹⁻¹³. The PTBD is performed as a preoperative procedure for resectable malignancies, prior to neoadjuvant chemotherapy or as a palliative technique⁷. Indications of percutaneous management of malignant biliary obstruction include high biliary obstructions, failed endoscopic drainage, post-operative cases with biliary obstruction, recurrent malignancies and multiple segment strictures¹⁴. There are no absolute contraindications for PTBD of MBO. Relative contraindications are hemorrhagic disorders, allergy to iodinated contrast agents and ascites¹⁴. Although safe, PTBD of malignant biliary obstruction is

associated with complications, which can be immediate or late⁷. The incidence of complications of PTBD ranges from 8%-42%¹⁵. The complications can be categorized into early (occurring within 30 days) and late. Early complications, with exception of pain, are seen in about 25%-50% of patients of which about half were procedure related¹⁶⁻²⁰. The complications include pain at the site of puncture (more common with rightsided punctures), bile leak with risk of biliary peritonitis and biloma formation, hemorrhage including haemobilia, biliovenous fistula, arterial injury, cholangitis and septicaemia, acute pancreatitis and catheter related problems like kinking or dislocation. The right lobe punctures are painful as the needle has to traverse the intercostal space. Left lobe punctures are associated with higher risk of bile leak and thus biliary peritonitis which may cause acute abdomen. Right sided punctures are also associated with the risk of pneumothorax and hemothorax. The rates of complications are lower with metallic stents compared with plastic stents (16% vs 29%)²¹. Vascular injury during the procedure can be arterial or venous. Arterial injury occurs in 1%-2% of cases and is more commonly associated with 18-gauge puncture needles and placement of three or more catheters in a single day^{22,23}. Left sided punctures are associated with higher incidence of hemorrhagic complications and is due to the lack of tamponading effect in left lobe punctures^{22,24}. The hemorrhage usually resolves spontaneously, and may need temporary clamping of the catheter. If it is persistent, CT angiography should be done and if it shows active contrast extravasation or pseudoaneurysm, treatment by embolization is needed. Biliovenous fistulas present with hemorrhage in the catheter or hemobilia and can be diagnosed on cholangiogram with filling of portal venous or hepatic venous radicles. They can be managed by temporary catheter clamping or by changing the catheter to a larger bore catheter¹⁶. Late complications include cholangitis, liver abscess, septicaemia, drainage catheter or stent blockage. Stent occlusion could be due to tumor ingrowth, tumor overgrowth or sludge.

The data of PTBD procedure in MBO from India are limited.

So we planned a prospective study to evaluate the efficacy and safety of PTBD in patients with malignant biliary obstruction.

MATERIALS AND METHOD

Aims and objective:

- 1) To study the efficacy and safety of percutaneous transhepatic biliary drainage in malignant biliary obstruction.
- 2) To evaluate the technical and clinical success of the procedure

Inclusion criteria:

- 1) Confirmed diagnosis of malignant biliary obstruction
- 2) Patients who gave consent for the procedure

Exclusion criteria:

- 1) Refusal to participate in the study
- 2) Patients with massive ascites
- 3) Patients with bleeding diathesis

Study design, study period and sample size:

From June 2018 to Nov 2019, data of all patients with malignant obstructive jaundice, who have undergone PTBD was analysed.

Statistical analysis:

The Wilcoxon signed rank test was used for comparison of non categorical variables (pre and post intervention bilirubin levels). The Kaplan–Meier survival curves will calculate the cumulative overall survival and the primary patency rates. The level of statistical significance is set at $P \leq 0.05$.

Following data was analysed:

A) History

Clinical history was analysed with particular reference to abdominal pain, pruritus, fever, anorexia, weight loss, and duration of symptoms. The patients underwent quality of life (QOL) assessment as well as performance status assessment using the European Organisation for Research and Treatment of Cancer QOL questionnaire version 3.0, based on 30 questions (EORTC QLQ C30)²⁵ and ECOG performance status scale²⁶ respectively

B) Laboratory

Complete blood count, Liver function tests (LFTs) (total bilirubin, direct bilirubin, indirect bilirubin, alanine transferase, aspartate transferase, alkaline phosphatases and total protein) and coagulation profile was analysed in all patients.

C) Imaging

Ultrasonography (USG), triple phase computed tomography and/or magnetic resonance imaging with magnetic resonance cholangiopancreatography was also analysed. Images were analyzed for: cause of obstruction (gallbladder carcinoma, cholangiocarcinoma, pancreatic/periampullary carcinoma, recurrent/post cholecystectomy gall bladder carcinoma and peri portal nodes) and level of obstruction whether hilar or nonhilar obstruction. For hilar obstruction Bismuth-Corlette classification was used. The criteria used for unresectability are those as described by Kumaran *et al*²⁷.

The diagnosis of obstructive jaundice was established on the basis of LFTs (increased serum bilirubin and alkaline phosphatase levels) and an abdominal USG showing dilated intrahepatic radicals. The diagnosis of malignancy was established preoperatively by clinical features, imaging studies and was confirmed by either an USG guided fine needle aspiration cytology (FNAC) / trucut biopsy from mass whichever possible. After the clinical, laboratory, and radiological investigations were completed, patients were offered the option of PTBD, a palliative method of treatment. Patients were informed about the procedure and related complications in detail and written informed consent were obtained. The procedures were performed with USG and fluoroscopic guidance. After the completion of the procedure, the patients were kept under observation in the gastroenterology department and closely followed for any immediate procedure related major or minor complications.

Follow up:

After the placement of catheter / stent and if there was no major complication during observation, the patients were discharged and called for regular follow up at 1 week, 1 and 6 months. Follow up of each patient was based on outpatient examinations and telephone interviews.

Analysis:

Technical success, clinical success, stent patency, survival and complication rates were recorded.

Technical success:

Technical success was defined as the successful deployment of the stent / internal external drainage tube in

the appropriate position resulting in drainage of the respective bile ducts.

Clinical success:

Clinical success was defined by a decrease in serum bilirubin level of more than 20% relative to baseline within 1 week after stent insertion.

Stent / catheter patency:

Stent/catheter patency period was defined as the interval between PTBD / stent placement and obstructive jaundice recurrence. Stent / Catheter block was diagnosed if the reappearance of jaundice after it had subsided. It was confirmed by one of the following:

- a) USG or CT demonstration of redilatation of bile duct
- b) Cholangitis

If stent / catheter occlusion does not occur during a patient's lifetime, the patency was considered equal to the period of survival.

Survival:

Survival (in days) was calculated from the day of intervention until death or last follow up.

Complications:

These were divided into major and minor categories according to the reporting standards of the Society of Interventional Radiology.

- a) Major complications included sepsis or cholangitis, hemorrhage requiring blood transfusion, abscess formation, peritonitis, cholecystitis, pancreatitis, pneumothorax, pneumonia, pleural infection, sepsis, stent / catheter migration and death.
- b) Minor complications included pain, self limiting haemorrhage, biliovenous fistula, sub capsular biloma.

Quality of life assessment:

QOL was assessed by EORTC QLQ C30 prior to the treatment and after 1 month of the treatment. The QLQ C30 is composed of 30 questions with a scale range from mild to severe measured on a scoring scale, and the questions are grouped together into two groups as described below.

- Functional 15 questions are under functional group
- Symptom 13 questions are under symptomatology group

- Global 2 questions are under global group.

Interpretation of quality of life scoring system :

A high score for a functional scale represents a poor level of functioning and an improvement in functional status is determined by a decrease in score.

A high score for the global health status / QOL represents a high QOL and an improvement in global status is determined by an increase in score.

A high score for a symptom scale / item represents a high level of symptomatology / problems and an improvement in symptomatology status is determined by a decrease in score.

The QOL questionnaire has been translated into Hindi and validated for use among Indian patients. The QOL was assessed at 1 month post treatment.

RESULTS

101 patients were planned for PTBD during the study period.

Females were 55 (54.45%) and males were 46 (45.55%).

Mean age was 55.5±22 years.

97 patients (96%) underwent PTBD for palliation, four (4%) underwent as required for pre-operative drainage.

Indications for PTBD:

- a) Severe pruritus refractory to medical management in 68 patients (67.3%).
- b) Cholangitis in 33 patients (32.6%)
- C) Pre-operative drainage (4%) as there was expectant delay in surgery

Cause of biliary obstruction:

Cause of malignant biliary obstruction (MBO) was carcinoma gallbladder in 77 patients (77.7%), cholangiocarcinoma in 10 patients (9.9%), carcinoma head of pancreas in 7 patients (6.9%), periampullary carcinoma in four patients (3.9%) and secondaries at porta in three patients (3.2%). (Table 1)

Type of block:

Type of block was hilar in 90 patients (89.1%) and lower end block in 11 patients (10.89%). Hilar block was type 1 in 3 (2.9%) patients, type 2 in 36 (35.6%) patients, type 3 in 42 patients (41.6%) and type 4 in nine patients (8.9%). (Shown in table 1)

Table 1: Distribution of patients according to cause of MBO and type of hilar block

Cause of MBO	Number (percentage)	Block –Type (Number)
Carcinoma gallbladder	77(77.7%)	Type 2 hilar block- 33
		Type 3 hilar block- 38
		Type 4 hilar block-6
Cholangiocarcinoma	10 (9.9%)	Type 1 hilar block- 3
		Type 2 hilar block-3
		Type 3 hilar block -1
		Type 4 hilar block- 3
Carcinoma head of pancreas	7 (6.9%)	Lower CBD block -7
Periampullary carcinoma	4 (3.9%)	Lower CBD block-4
Secondaries at porta	3 (3.2%)	Type 3 hilar block-4

Table 2: Baseline laboratory parameters

Serum bilirubin	19.9 ±12 mg%
Conjugated fraction	9.5±7.4 mg%
AST	119± 200 U/L
ALT	88± 110 U/L
ALP	666±940 IU/L
Haemoglobin	10.64±2.5 gm%
TLC	12670±13900 mm ³
Prothrombin time	19±6 seconds

97 patients had unresectable disease. Most common criteria for unresectability was metastatic disease followed by locally advanced disease (shown in table 3)

Table 3: Distribution of patients according to unresectability on imaging

Criteria for unresectability	Number of patients ,n=97(percentage)
Vascular invasion	20 (20.6%)
Locally advanced disease	34 (35.05%)
Metastasis	43 (44.3%)

PTBD approach:

Right anterior approach in 54 patients (58%) and subxiphoid in 37 patients (39.7%). So unilateral approach was used in majority of our patients (97.8%), whereas bilateral approach was used in 2 (2.15%) patients in our study. The bilateral approach was used in those patients with blocked confluence, in which the contralateral ducts were inadvertently opacified during cholangiography, as these patients were at high risk of cholangitis if left undrained. The majority of patients had a high obstruction involving the primary confluence and hence there was unilateral drainage in the majority of the patients.

PTBD and stent internalization with 7 Fr DPT stent was done in 3 patients (2.9%) with lower CBD block.

PTBD guided rendezvous in 4 patients (3.96%).

ERCP Failure:

ERCP failure was in 25 patients (24.75%).

Gastric outlet obstruction (11), failed CBD cannulation (9), tight stricture at hilum (4) and altered anatomy (1) were reasons for ERCP failure

Technical success:

93 patients underwent the successful deployment of the stent / internal and external drainage tube in the appropriate position resulting in drainage of the respective bile ducts. So technical success in our centre is 92.07%.

Clinical success:

88 patients had decrease in serum bilirubin level of more than 20% relative to baseline within 1 week after stent insertion. Five patients had catheter mis-placement within one week resulting in increase in serum bilirubin, thus not fulfilling criteria for clinical success. So clinical success is 94.6%.

Complete follow up was available in 85 patients at 1 month, and 8 patients expired within 1 month either due to disease progression or co morbid conditions. Among 8 patients who died within one month, the latest bilirubin levels were available for 6 patients only, just before death and so these values were recorded as 1 month follow up. Hence, a total of 91 patients were analyzed at 1 month.

Serum bilirubin levels were measured before and after treatment. The pre-interventional values and the final post-interventional values at 1 month were recorded. Mean serum bilirubin level before PTBD was 19.9 ± 12 mg/dl (range 10–34.5 mg/dl) and after the procedure at 1 month was 4.2 ± 6 mg/dl (range 2–16 mg/dl). The mean difference in total bilirubin was 15.7 mg/dl, and the percentage reduction of total bilirubin level was 78.9% from the baseline total bilirubin level. The difference in the pre and post intervention bilirubin levels as estimated with Wilcoxon signed rank test is found to be statistically significant with 95% confidence interval as estimated by Hodges Lehmann estimator (Std. W= -8.3, CI=-17.2- -14.5, $P < 0.05$).

For the analysis of patency rates and survival rates, patients were stratified into the two groups based on the post PTBD bilirubin levels at 1 month (serum bilirubin < 4 mg / dl vs. 4 mg / dl or more).

Around two third (64.8%) patients had serum bilirubin level less than 4 mg / dl and 35.2% patients had serum bilirubin levels ≥ 4 mg / dl post PTBD at 1 month (Table no. 4).

Table 4: Distribution of patients according to the absolute bilirubin level at 1 month

Bilirubin Level (mg/dl)	No. of patients	Percentage
< 4	59	64.8
≥ 4	32	35.2
Total	91	100

Stent/catheter patency:

Stent/catheter patency period was defined as the interval between PTBD/stent placement and obstructive jaundice recurrence. As PTBD was successfully carried out in 93 patients, recurrence of jaundice occurred in 82 patients due to stent blockage. 11 patients had functional stent and did not experience any rise in the bilirubin during the study period.

The range and mean patency of PTBD catheter were 14 to 120 days and 51 ± 46 days.

Table 5: Distribution of the patients according to the patency.

Patency (Days)	Number of Patients (%)	Percentage
<30 days	11	13.4
30-59	35	42.7
60-119	35	42.7
≥120	1	1.2
Total	82	100

Relation between patency rate and amount of bilirubin reduction.

In the patients with serum bilirubin level < 4mg / dl the mean patency was 54.1 ± 6.6 days and in the patients with serum bilirubin level ≥ 4 mg/dl the mean patency was 49.8 ± 8.4 days. There is mean difference of 4.3 days and it is statistically insignificant at 95% confidence level ($\chi^2=0.54$, $df=1$, $p=0.46$). The Kaplan-Meier curve is shown in the graph. (Figure 1)

Quality of life assessment

Of the 8 patients who died within 30 days, the latest QOL scores were not available for these patients, just before death. Hence the QOL scores were calculated for 85 patients at 1 month follow up. The pre-interventional values and the final post-interventional values were recorded. There was an improvement in the QOL symptomatic, which was statistically significant (P 0.04). QOL functional also improved after PTBD significantly (p 0.037.) but QOL global improves after PTBD but difference was not statistically significant. Pre and post PTBD QOL values are depicted in Table 6.

Table 6: Quality of life assessment before and after PTBD

Status	QOL Functional	QOL symptomatic	QOL global
Pre- PTBD	41.67±13	38.8±13.48	4.8±3.4
Post- PTBD	24.73±8.4	23.12 ±7	9.46±2.5
P value	0.037	0.04	0.2

Stent / catheter patency:

Stent / catheter patency period was defined as the interval between PTBD / stent placement and obstructive jaundice recurrence.

Stent / catheter patency period in our study was 51 ± 46 days (range 14 -120 days).

Complications:

A) Early complications:

Minor complications:

Pain at puncture site in 22 patients (21.8%), mild hemorrhage in 7 patients (7.5%), transient blood tinged bile in 8 patients (8.6%), so excluding pain at puncture site, 16.1% of our patients had minor complications.

Major complications:

Accidental removal of PTBD catheter in 5 patients (5.4%). Accidental removal of PTBD catheter leads to cholangitis and recurrence of symptoms. This was managed with repeat PTBD.

B) Late complication:

All of these complications were major. Late complications were accidental removal of PTBD 28 times (30.1%) in 21 patients, meaning thereby some patients had PTBD misplacement multiple times.

Catheter blockage in 7 patients (7.5%), stent migration in 2 patients (2.15%).

Accidental removal of PTBD leads to cholangitis (21 patients), perihepatic collection (2 patients) and leak from PTBD site (5 patients). Cholangitis was managed with repeat PTBD in 18 patients, ERCP and biliary SEMS placement in 3 patients. 2 patients with perihepatic collection underwent percutaneous drainage for perihepatic collection along with repeat PTBD.

Catheter blockage leads to cholangitis (6 patients) and perihepatic collection (1 patient). Catheter blockage was managed with flushing of PTBD catheter with normal saline in 2 patients and upsizing of PTBD catheter in 3 patients, stent internalization with 7 Fr DPT in 2 patients. One patient required additional percutaneous drainage for perihepatic collection.

Stent migration leads to cholangitis (2 patients) which was managed with placement of PTBD catheter and removal of internally migrated stent.

So major (both early and late major) complications in our centre were 45.15%.

Survival:

81 patients out of 93 who underwent PTBD, died during the study period (Table no.5); the mean length of survival in study group was 74 ± 90 days (Range 14- 270

days). 12 patients were alive till last follow up on 31st December 2019. Calculated median survival time was approx 70 days.

Table 7: Distribution of patients according to the survival (n=93)

Survival (days)	Number of Patients	Percentage
≤30	8	8.6
31-180	70	75.3
>180	15	16.1
Total	93	100

Relationship between survival rates of patients and reduction of serum bilirubin levels

In 59 patients (64.8%) with post PTBD bilirubin levels of less than 4mg/dl at 1month, the mean survival was 81.4 ± 15.6 days and in the remaining 32 patients (35.2%) with post PTBD bilirubin levels of ≥ 4 mg/dl at 1month, the mean survival was 70.4 ± 7.6 days. Kaplan-Meier log rank (Mantel-Cox) survival analysis showed that there was no statistical significance between the survival rates of the patients when they were grouped according to the post PTBD bilirubin levels ($\chi^2=0.39$, $df=1$, $p=0.532$) (Figure 2).

DISCUSSION

Malignant obstructive jaundice is a common clinical problem and can occur due to variety of causes as described earlier¹. GBC is the most common cause of malignant biliary obstruction in our country. Most of these patients present with obstructive jaundice caused by biliary obstruction²⁸. As majority of the patients are not candidates for curative resection, the therapeutic goal is often palliative, given the short life expectancy.

PTBD is a well established procedure used in patients with malignant biliary obstruction for decompression of intra and extra hepatic bile ducts^{15,29}.

In our study, most frequent diagnosis was GBC (77.7%), followed by cholangiocarcinoma (9.9%), pancreatic (6.9%), periampullary carcinoma (3.9%), and secondaries at porta from unknown primary (3.2%). Our results were similar to study conducted by Shivanand Gamanagatti et al³⁰.

Unilateral approach was used in majority of our patients (97.8%), similar to study conducted by Shivanand Gamanagatti et al³⁰.

Technical success in our centre is 92.07%. In the study reported by Saluja et al¹⁹ the technical success achieved was 93% in the PTBD group, whereas it was 82% in the endoscopic stenting group.

Technical success was 100% in a study done by Shivanand Gamanagatti et al³⁰.

Clinical success

Clinical success was assessed in 93 patients in which there was technical success. 88 patients had decrease in serum bilirubin level of more than 20% relative to baseline within 1 week after stent insertion. Also five patients had catheter misplacement within one week resulting in increase in serum bilirubin, thus not fulfilling criteria for clinical success. So clinical success was 94.6%. The overall clinical success rate was 89.97% in a study done by Shivanand Gamanagatti et al³⁰.

We also assessed the difference in the pre and post-intervention bilirubin levels as estimated was Wilcoxon signed rank test, which was statistically significant similar to the study done by Shivanand Gamanagatti et al³⁰.

Quality of life

Successful biliary drainage alleviates jaundice, improves liver function, and has a positive impact on QOL²⁸. There was an improvement in the QOL symptomatic, which was statistically significant ($P=0.04$). QOL functional also improved after PTBD significantly ($p=0.037$) but QOL global improves after PTBD but difference was not statistically significant.

Relation between patency rate and amount of bilirubin reduction:

In the patients with serum bilirubin level < 4 mg / dl the mean patency was 54.1 ± 6.6 days and in the patients with serum bilirubin level ≥ 4 mg / dl the mean patency was 49.8 ± 8.4 days. There is mean difference of 4.3 days and it is statistically insignificant at 95% confidence level.

However in a study done by Shivanand Gamanagatti et al³⁰ patients with serum bilirubin < 4 mg / dl, the mean overall patency was 150.2 days, whereas in patients with serum bilirubin > 4 mg / dl, the mean overall patency was 79.89 days with a mean difference of 70.1 days, which was statistically significant ($P < 0.001$). This may be due to frequent misplaced PTBD catheter in our patients and less internalizations in our patients.

Survival:

81 patients died during the study period, survival in these patients was 74 ± 90 days (Range 15- 270 days). The estimated mean length of survival for the entire patient population was 116.8 days (range 2–445 days) in a study done by Shivanand Gamanagatti et al³⁰.

Kaplan-Meier log rank (Mantel-Cox) survival analysis showed that there was no statistical significance between the survival rates of the patients when they were grouped according to the post PTBD bilirubin levels ($\chi^2=0.39$, $df=1$, $p=0.532$) (Figure 1).

However in a study by Shivanand Gamanagatti et al³⁰, univariate Kaplan–Meier (log rank) survival analysis revealed a statistically significant difference in the survival rate when patients were stratified according to the post-stenting bilirubin levels (serum bilirubin < 4 mg / dl vs > 4 mg / dl) ($P=0.007$).

We did not see such survival benefit, may be because PTBD is a palliative procedure, improves quality of life but not survival. And survival in MBO is related to underlying malignancy.

Stent / catheter patency:

Stent / catheter patency period in our study was 51 ± 46 days (range 14 -120 days)

Mean primary patency was 113.2 days (range 2–445 days) in a study done by Shivanand Gamanagatti et al³⁰.

Complications:

16.1% of our patients had minor complications similar to a study done by Shivanand Gamanagatti et al who reported them to be 14.3%³⁰.

We also reported cholangitis as early major complications in five patients (5.4%) due to accidental misplacement of PTBD. Our patients were successfully managed with repeat PTBD.

Major complications occurred in four patients (8.1%) in a study by Shivanand Gamanagatti et al³⁰. In all the patients, complications developed 2–3 days after the procedure: All four patients developed severe sepsis leading to death, and all were caused by severe cholangitis, not responding to antibiotics.

No immediate major complications in the form of hemorrhage requiring a blood transfusion, shock, or procedure related death were observed in our study,

similar to study done by Shivanand Gamanagatti et al³⁰, thus highlighting safety of the procedure in expert hands.

Catheter blockage was noticed in 7 patients (6.5%) of our patients. Time to occlusion ranged between 30 to 60 days (mean 45 ± 40 days). Catheter blockage was managed with flushing of PTBD catheter with normal saline in 2 patients and upsizing of PTBD catheter in 3 patients, stent internalization with 7 Fr DPT in 2 patients. One patient required additional percutaneous drainage for perihepatic collection.

In a study done by Shivanand Gamanagatti et al³⁰ eight patients developed catheter occlusion in the total duration of 6 months (16.3%). Time to occlusion ranged between 10 and 135 days (mean 52.6 days). All occlusions were managed conservatively. None of the patients underwent pre intervention.

In the literature, rates of minor and major complications range between 8% and 23% and between 2% and 20%, respectively^{15,16}.

CONCLUSION

Most common cause of malignant biliary obstruction is still carcinoma gallbladder. Percutaneous management of malignant biliary obstruction is a good method for palliation with good technical success (92%) and clinical success (94.6%). The difference in the pre and post intervention bilirubin levels at 1 month as estimated with wilcoxon signed rank test is found to be statistically significant. Unilateral approach was used in majority of our patients (97.8%) as drainage of 25%-30% of normal liver is adequate to improve jaundice and liver functions. PTBD is a good alternative in ERCP failure patients (25% in our study). Successful biliary drainage alleviates jaundice, improves liver function, and has a positive impact on QOL. Stent / catheter patency period in our study was 51 ± 46 days (range 14 -120 days). Survival in our patients was 74 ± 90 days (Range 15- 270 days). Kaplan-Meier log rank survival analysis showed that there was no statistical significance between the survival rates of the patients when they were grouped according to the post PTBD bilirubin levels. However complications reported by us were higher than reported in literature.

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ORIGINAL ARTICLE

Psychological Impact of COVID-19 Pandemic among General Population in Rajasthan: A study

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ABSTRACT

Background: The pestilent and infectious nature of COVID-19 pandemic pose a unique medical challenge to the humanity in recent times. In the absence of an effective counter measure, imposition of mass lockdown seems to be the only way, but possess an undesirable side effect of posing a negative psychological impact among general population.

Aim: To assess the psychological impact of COVID-19 pandemic on general population in Rajasthan after one and half month of unlock from nationwide mass lockdown.

Materials and Method: It was an online survey, conducted using Google Forms via a link sent through Whatsapp. The questionnaire used for the study was self-designed and tailor made according to the study requirements. A total of 200 responses were received during the stipulated cut off time.

Results: Near about one fourth (25.7%) of the respondents reported as having disturbed sleep-wake cycle in the past five months. Majority of the respondents were worried more than usual about future of themselves and their family members (61.4%) and were worried about the financial loss that incurred during the period of lockdown (52.5%). Majority (52.9%) of the respondents agreed that COVID-19 pandemic had affected their mental status to some extent. One third (37.9%) and two-fifth (39.2%) of respondents found that COVID-19 pandemic had threatened their existence and they found it difficult to adjust to the new routine during 21-day lockdown period, respectively.

Conclusion: The index survey suggested that worry and sleep disturbances were common in

respondents after one and half months of unlock but less than what happened at the start of pandemic. The pandemic had threatened the existence of respondents to greater extent but now respondents were starting to get adapted to a “new normal”.

Keywords: COVID-19, Lockdown, Psychological Impact

INTRODUCTION

The corona virus infection or COVID-19 outbreak is one of the biggest medical challenges to mankind in recent times. The outbreak of COVID-19 infection started in China in December 2019 and spread to almost all the countries of the world by January–February 2020¹.

The World Health Organization (WHO) declared COVID-19 as a pandemic on March 11, 2020 and cases are still on a rise in the world¹.

In India, cases of COVID-19 started to rise by the 2nd week of March 2020, and by March 31, 2020, more than 1,356 cases were reported with 46 deaths². Now according to India COVID-19 Tracker (last updated 31 July 2020) confirmed cases are nearly 16 lakh 43 thousand with 5 lakh 50 thousand active cases and 35 thousand 8 hundred deaths.

The spread of corona virus infection occurs by droplet transmission. For prevention of spread of this deadly disease “lockdown” was the only available practical and implementable strategy. The Prime Minister of India declared “Lockdown” for 21 days on 25th March 2020 which was further extended with relaxations till 31st May 2020 in phases. “Lockdown” was an emergency protocol, which basically means preventing public from moving from one area to the other hence restricting the citizens from coming outside and help in maintenance of

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social distancing. In this scenario, all educational institutions, shopping arcades, factories, offices, local markets, transport vehicles, airports, railways, metros, buses, etc., were completely shutdown except emergency services such as hospitals, police stations, fire stations, petrol pumps, groceries stores and stores catering eatables. Moreover, the lockdown provided ever so precious time for the administration to arrange for proper beds including ICU beds and other medical facilities such as drugs, ventilators etc. Since there was a lack of effective drugs & vaccines against novel corona virus, the lockdown provided time for development of these. Also, the lockdown has delayed the peak of COVID-19 case load. While lockdown can serve as an effective strategy for prevention of corona virus infection it can have some degree of psychological impact on public. It is well known that quarantine/isolation for any cause are associated with significant mental health problems ranging from anxiety, fear, depressive symptoms, sense of loneliness, sleep disturbances, anger, etc in immediate few days of isolation followed by symptoms of post traumatic stress disorder and depression even after 3-4 weeks of discharge³. These symptoms were also reported during Pandemic caused by SARS in 2003.

After initiation of step by step unlock of the lockdown by the administration, movement of general public has been restored to near normal although with a rise in the number of new cases. A sense of panic has set in among the general population alarmed by the increasing number of positive cases with each passing day and by the rumours & myths about COVID-19 that are being circulated on social media platforms. COVID-19 poses a serious threat as a contagious illness, as a threat to physical and psychological integrity of a person and in the long run, has a potential of causing huge socioeconomic impact⁴.

Aim of the study-The aim of the present study is to look into the psychological impact of COVID-19 pandemic and the administrative measure of “lockdown” on general population after five months of the COVID-19 outbreak.

MATERIAL AND METHODS

An online survey was conducted using Google Forms via a link sent using whatsapp. Google forms have an advantage of submitting responses anonymously and also it mitigates the need of physical contact with the persons to be surveyed thus ensures social distancing. The

investigators can only see the responses but not the name of the person who sent it. The link was first circulated on 20.07.2020 at 22:16:11 IST and kept open for responses till 01.08. 2020 at 10:28:21 IST. Daily reminder was sent. The survey invitation clearly stated that the participants will have the right, not to participate in the survey and participation in the survey will imply their consent. The survey questionnaire normally took around 5-7 min to complete. A total of 200 responses were received by the stipulated cut-off time

Inclusion and exclusion criteria

The participants with age more than 20 years of both gender who were capable of reading and understand English, had internet connection and whatsapp installed on their phone, were included for the study. Participants who were unwilling to respond to survey were excluded from the study.

Tool used

A self designed tailor made questionnaire was used for the purpose of the study. The questionnaire included questions about sociodemographic profile of the respondents and psychological impact of COVID-19 pandemic on the respondents

Statistical analysis

Descriptive analysis was done and results were expressed in terms of numbers and percentage.

Table 1: Sociodemographic profile of the respondents

Variables	Percentage (number of responders)
Age (years)	
20-30	9.3% (19)
30-40	22.1% (44)
40-50	40.2% (80)
50-60	15.2% (30)
60-70	8.8% (18)
70-80	4.4% (9)
Gender	
Male	47% (94)
Female	53% (106)
Profession	
Health care provider	39.1% (78)
Home maker	13.7% (28)
Banking sector	10.7% (22)
Teacher	8.6% (17)
Businessman	11.2% (22)
Student	4.2% (8)
Private job	6.4% (13)
Others	6.1% (12)

Level of education	
10 th pass	2.4% (5)
12 th pass	4.4%(9)
Graduate	26.6% (53)
Postgraduate	61.1% (122)
Post doctoral	5.5% (11)
Residence	
Urban	60.6% (121)
Metrocity	28.6% (57)
Semiurban	8.8% (18)
Rural	2% (4)

Table 2: Psychological impact of corona virus disease 2019 pandemic on the respondents

Variables	% (n)
Are you worried more than usual in last four months	70.8% (142)
Yes	29.2% (58)
No	
Are you preoccupied with idea of contracting COVID-19 during past four months	50%(100)
Yes	50% (100)
No	
Are you repeatedly thinking of getting yourself tested for presence of COVID -19 in your body (although you have no symptoms)	14.4% (29)
Yes	85.6% (171)
No	
Have your sleep cycle become disturbed in past four months	25.7% (51)
Yes	74.3%(149)
No	
Do you keep checking for fever with thermometer repeatedly in past four months	13.9%(28)
Yes	86.1% (172)
No	
Have you visited doctor on multiple occasions to rule out the symptoms of COVID-19 in past four months	3% (6)
Yes	97%(194)
No	
Are you afraid of testing COVID-19	25.9%(51)
Yes	74.1%(149)
No	
Are you checking daily details about COVID-19 spread	68.7% (137)
Yes	31.3% (63)
No	
Are you worried more than usual about future of yourself and family members in past four months	61.4%(123)
Yes	38.6% (77)
No	

Have you become more irritable than usual in past four months	33.2%(66)
Yes	66.8% (134)
No	
Are you worried about the financial loss that are incurring to you during period of lockdown	52.5%(115)
Yes	47.5% (85)
No	
Have you done routine blood tests in past three months to be sure that your health is OK	11.9% (24)
Yes	88.1%(176)
No	
Do you get more depressed after reading the whatsapp or facebook messages related to COVID-19 in past four months	34.7%(69)
Yes	65.3%(131)
No	
Do you get more worried after reading the whatsapp or facebook messages related to COVID-19 in past four months	48.5%(97)
Yes	51.5%(103)
No	
How are you spending time during lockdown	
Doing household chores	38.7%(77)
Watching movies	15.6%(31)
Work from home	27.6%(55)
Reading books	8.5%(17)
Others	9.6%(20)
Have you taken the help of psychiatry helpline to reduce your anxiety and depression during last four months	3.5%(7)
Yes	96.5% (193)
No	
Are you on any antidepressants/ antianxiety medications which has been started in past four months	2.5% (5)
Yes	97.5%(195)
No	
Are you taking any sleep medication for past four months	2.5%(5)
Yes	97.5%(195)
No	
How do you think COVID-19 pandemic has affected your mental status negatively	5.4%(11)
Has affected me to great extent	52.9% (106)
Has affected me to some extent	41.7%(83)
Has not affected me at all	
Do you find that COVID-19 pandemic has posed a threat to your existence	37.9%(76)
Yes	62.1%(124)
No	
Do you found it difficult to adjust to new routine during lockdown period	39.2%(78)
Yes	60.8%(122)
No	

RESULTS

71.6% of the respondents were below 50 years of age with majority of them falling in the age group of 40-50 years (40.2%), 39.1% respondents were health care providers, 61.1% were postgraduates and 60.6% were from urban locality.

Near about seven-tenth (70.8%) of the respondents felt worried in past four months which is more than what is considered to be the normal prevalence of worry in the community. Near about one-third (33.2%) of the respondents had a history of irritability in the past four months. Half of the respondents (50%) were preoccupied with the idea of contracting COVID-19 and one-seventh (14.4%) of the respondents repeatedly had a thought of getting themselves tested for the presence of COVID-19 despite having no symptoms. Relatively fewer respondents kept checking their fever with thermometer repeatedly (13.9%) and visited doctor on multiple occasions (3%) to rule out the symptom of COVID-19 and underwent routine blood tests (11.9%) to ensure that their health was normal in past three months. Nearly one fourth (25.7%) of the respondents reported having a disturbed sleep-wake cycle. Majority of the respondents (61.4%) were worried more than usual about their future and future of their family members and 52.5% were worried about the financial loss that incurred during the period of lockdown. One-third (34.7%) and half (51.5%) of the respondents got more depressed and worried, respectively after reading COVID-19 related news on social media. Majority of the respondents were spending time during lockdown either performing house-hold chores (38.7%) or working from home (27.6%). Only a minority of the respondents took help from Psychiatry helpline (3.5%). Among these, 2.5% were put on antidepressant and/or anti-anxiety drugs in the past four months and 2.5% reported consumption of sleeping pills for past five months. Majority (52.9%) of the respondents found that COVID-19 pandemic had an effect on their mental status to some extent. One third (37.9%) and two-fifth (39.2%) of respondents found that COVID-19 pandemic had threatened their existence and found it difficult to adjust to the new routine during 21-day lockdown period (25 March to 31st May), respectively.

DISCUSSION

The present survey assessed the psychological impact of COVID-19 on general population in Rajasthan nearly four months after 1st case was registered in India.

Nationwide Lockdown in India was enforced from 25th March 2020 and extended till 31st May 2020. Step wise Unlock was initiated from 1st June 2020 and the present survey was done using Google Forms in the state of Rajasthan after nearly one and half month of unlock.

Sociodemographic profile of the study participants suggested that majority of respondents were well educated, living in urban setting and were 40-50 years of age. 85.6% of respondents admitted that they were not thinking for getting themselves tested for the presence of COVID-19 without overt symptoms suggestive of the disease. This finding correlated with a similar observation obtained in a previous study⁴. The probable explanation to this might be the fear of contracting the disease and the ever so toilsome quarantine measures recommended by the administration along with pervasive social stigmata associated with diagnosis of COVID-19. In our study 13.9% of respondents kept checking for fever with a thermometer repeatedly in comparison to 9.7% respondents doing so as per a previous study⁴. As per the present study, 3% of respondents reported visiting doctor on multiple occasions for ensuring ruling out the symptoms of COVID-19 in comparison to a figure of 1.6% as reported in a previous study⁴. 11.9% of respondent underwent routine blood tests in past four months to assess their health status in comparison to 3.4% in previous study⁴. The above observations suggest an increase in awareness about COVID -19 among general population emanating possibly due to plethora of information available to them through various media platforms in due course of time. An increased trend of opting elective blood investigations by the respondents might also be attributed to the fact that a large proportion of respondents comprised of health care providers who supposedly had an easy access to the health care facilities and(or) were more vigilant about their health. On one hand, the respondents showed a higher tendency of going for blood investigations while on the other hand, demonstrated a strikingly low interest in opting for COVID-19 tests, like RT-PCR, indirectly implying a probable fear of quarantine measures and social stigma associated with being labelled as COVID-19 positive even among the health care providers.

61.4% respondents were worried more than usual either for their own future or future of their family in comparison to 71.8% participants reporting so in previous study⁴. 33.2% became more irritable than usual in past

four months in comparison to 37.1% in previous study⁴. 52.5% worried about financial loss during lockdown period in comparison to 69.6% in previous study⁴. This had been probably resulted since majority of respondents were health care providers and persons with businesses/occupations dependent on normal socioeconomic backdrop comprised a small group of respondents. Since salaries of healthcare workers were unfazed during the pandemic, their financial condition was less affected in lockdown period and hence resulting in lesser worries.

65.3% and 51.5% of respondents did not get depressed and worried after reading the Whatsapp or Facebook messages related to COVID-19 in past four months respectively in comparison to a correspondingly 45.2% and 34.7% participants in previous study⁴. The apparent difference might have been resulted possibly due to the timing of the survey wherein the previous study was conducted during the lockdown and the present survey underwent during a phase when unlock protocols are in practice by and large. Despite a steady rise in number of cases, the stress level has declined in the minds of people as exemplified by having 52.9% of respondents with a notion that COVID-19 pandemic had affected their mental status negatively to some extent in comparison to 64.9% participants having similar thoughts in previous study⁴. The prevalence of negative emotions in the study was found to be higher in comparison and might be the knee jerk reaction to the plethora of fake news related to COVID-19 circulating on social media. However 62.1% respondents in the present study did not find/acknowledged COVID-19 pandemic as a threat to their existence in comparison to 33.9% in previous study as majority of the respondents were from the fraternity of health care providers and were well educated and adapted to COVID-19 pandemic.

CONCLUSION

COVID-19 pandemic has created a setting of extraordinary socioeconomic and psychological challenge to mankind. The effect of COVID-19 pandemic has a propensity to last very long and the present survey was done to observe effect of COVID-19 pandemic on psychological wellbeing of mankind. The survey indicated that worry and sleep disturbances were common among respondents even after one and half months of unlock. The pandemic had threatened the existence of respondents to a greater extent but now respondents were starting to get adapted to a new normal.

Future direction

Future studies with large sample size should be done to assess the psychological impact of COVID-19 on larger population which can represent whole India. Similar studies can also be done on frontline health care workers, COVID-19 survivors, policemen and caregivers.

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ORIGINAL ARTICLE

The Effect of Storage Temperature of Whole Blood on Platelet Count – A Biophysical Perspective

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ABSTRACT

Introduction: Hematological examinations of blood samples are frequently analysed with significant time delay and this interval is a highly significant pre-analytic variable along with the storage temperature of blood samples. The present study aims to assess the variation in platelet count with time for samples stored at the real room temperature (30°-40°C), at 4°C and at 25°-27°C.

Materials and Method: Fifty apparently healthy young adults, aged 17-25 years were selected randomly, irrespective of their gender. Blood samples from the subjects were collected and stored in three storage settings: in a refrigerator (FT - 4°C), in a constant temperature bath containing water (PT -25°-27°C) and at room temperature (RT – 30°-40°C). The blood sample were analysed for absolute platelet counting (APC) repeatedly for five days. Room temperature samples were also done with an automatic cell counter. The pattern of fall in APC was observed and analysed.

Results: The mean platelet counts for all the samples stored showed an overall nonlinear decrease in counts with time. The FT, RT and PT cell count decreased rapidly during the initial 6 hours, 15-20 hours and 25 hours respectively. Thereafter the fall slowed down. In contrast, the counts made on automatic cell counter showed the least variation over the duration of study.

Conclusion: The platelet counts and their rate of fall is predominantly a function of platelet metabolism at higher temperatures however their activation and adhesion occurs at lower temperatures.

Keywords: Platelet, complete blood counts, thrombocytopenia.

INTRODUCTION

Hematological examinations of blood samples, though indicated to be made as soon as possible after sampling, are rarely made immediately. In the real scenario, blood samples are frequently delivered to the clinical laboratory after a significant post-collection interval labeled as the "DEAD TIME" of approximately 4 hours^{1,2}. On weekends this interval may exceed 72 hours.² This interval is a highly significant pre-analytic variable along with the storage condition of blood samples, and thus, remains an intriguing issue for the stability of hematological parameters.

Manufacturers of automated analyzers and published literature often cite that specimens kept at either room temperature or at 4°C (refrigerated) for up to 24 hours generally yield reliable results for complete blood cell count (CBC) and automated differential leucocyte count²⁻⁴.

However, specific information concerning the suitability or unsuitability of specimens older than one or two days for various tests and the effect of such delay on the reliability of test results is limited, particularly in the recent literature².

When the effect of such delay is coupled with the high temperature settings of tropics the suitability of the specimen becomes highly questionable with an increasing probability of unreliability of test results with the storage of samples at increasing temperature, even for short time periods.

The present study aims to assess the variation in platelet count, with time, and the reasons thereof, in healthy young adults, specially at high room temperatures

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of tropical summer for samples stored at the real room temperature, at 4°C and at 25°-29°C.

MATERIALS AND METHOD

The study was conducted in the Department of Physiology, Government Medical College, Kota Rajasthan. As the study was concerned with the effect of the "real" room temperature, specially the high temperatures, the study was performed in warm, dry days of April to July when room temperature exceeds 30°C.

After obtaining the approval of the institutional ethical committee, fifty apparently healthy young adults, aged 17-25 years were selected randomly, irrespective of their gender and their written informed consent was taken to participate in the study. Subjects who were smoker, alcoholic, having infections (specially viral, within one month) or any other acute or chronic illness were excluded.

The subjects were divided into ten groups having five persons in each group. Blood samples from each group was studied for five days. Blood samples were collected by drawing 10 ml venous blood from the antecubital vein and immediately anticoagulated in three EDTA vials. After immediate mixing, one vial was placed in a refrigerator (4°C), (*FT sample*) and another in a constant temperature bath containing cold water (25°-29°C), (*PT sample*). The blood from the third vial (*RRT sample*), was immediately subjected to platelet counting using light microscope and hemocytometer (improved Neubauer's chamber). All parts of the sample were subjected to counting everyday for five days. The timing of counting was as follows:

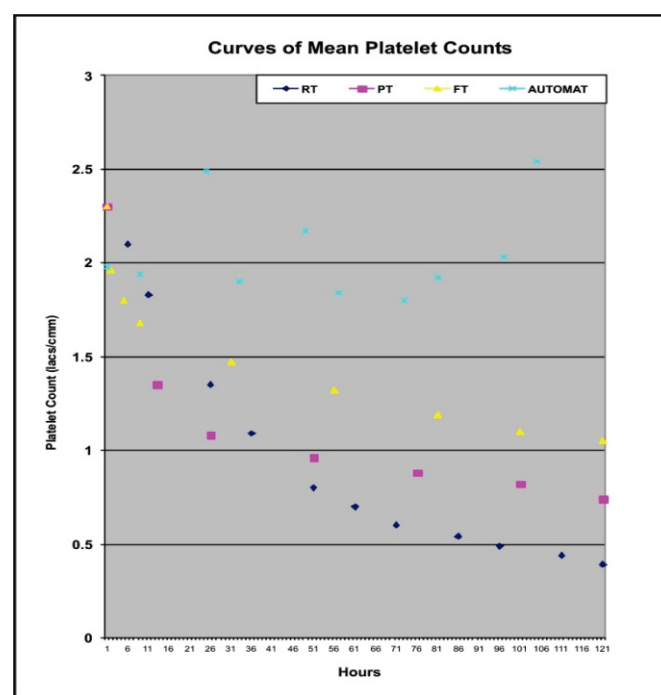
- RRT samples: 0.5, 5, 10, 25, 35, 50, 60, 70, 85, 95, 110 and 120 hours.
- PT samples: 0.5, 12, 25, 50, 75, 100 and 120 hours.
- FT samples: 0.5, 1, 4, 8, 30, 55, 80, 100 and 120 hours.

- RRT samples (with automatic cell counters): 0.5, 8, 24, 32, 48, 56, 72, 80, 96, 104 hours.

The platelet count was done by improved Neubauer's chamber. Platelet counts were performed three times on the same sample and an average of the three counts was used for analysis to minimize the manual error in counting. Refrigerated samples were placed at room temperature for 15 minutes before counting. The time of counting was measured from the time point at which the blood was drawn. All the RRT samples were also done on automatic cell counter repeatedly for comparison with the hemocytometer counts. Room temperature was measured at 6 hour intervals throughout the study. In view of the characteristics of the data set the summary measures method was used for analyzing the data from the study⁵⁻¹¹.

RESULTS

The mean platelet counts for all the samples stored showed an overall nonlinear decrease in counts with time.



RRT samples	0.5 hr	5 hr	10 hr	25 hr	35 hr	50 hr	60 hr	70 hr	85 hr	95 hr	110 hr	120 hr
Mean PC (lacs/cmm)	2.30	2.09	1.84	1.35	1.09	0.80	0.70	0.60	0.54	0.48	0.44	0.39
SD	0.49	0.54	0.48	0.41	0.36	0.27	0.23	0.21	0.19	0.17	0.20	0.21
CV	21.44	25.72	26.16	30.46	33.09	33.82	32.65	34.21	35.11	34.54	45.61	53.94

PT samples	0.5 hr	12 hr	25 hr	50 hr	75 hr	100 hr	120 hr
Mean PC (lacs/cmm)	2.30	1.34	1.08	0.96	0.88	0.81	0.74
SD	0.49	0.32	0.25	0.22	0.20	0.28	0.32
CV	21.44	23.58	22.89	22.68	22.33	34.69	43.67

FT samples	0.5 hr	1 hr	4 hr	8 hr	30 hr	55 hr	80 hr	100 hr	120 hr
Mean PC (lacs/cmm)	2.30	1.96	1.80	1.68	1.47	1.32	1.19	1.10	1.05
SD	0.49	0.50	0.45	0.45	0.39	0.35	0.31	0.26	0.32
CV	21.44	25.29	24.79	26.88	26.90	26.25	25.76	23.92	30.23

Auto RRT	0.5 hr	8 hr	24 hr	32 hr	48 hr	56 hr	72 hr	80 hr	96 hr	104 hr
Mean PC (lacs/cmm)	1.98	1.94	2.49	1.90	2.17	1.84	1.80	1.92	2.03	2.54

Data for Summary Measures Analysis							
Time to reach 75% of initial platelet count (t ₇₅)				Rate of decrease in platelet counts (Regression coefficients)			
	t ₇₅ RT	t ₇₅ PT	t ₇₅ FT		RT _{RC}	PT _{RC}	FT _{RC}
Mean	12.84	4.72	10.34	Mean	-0.035	-0.049	-0.02
SD	6.12	1.95	11.46	SD	0.009	0.011	0.005
CV	47.68	41.29	110.8	CV	-26.714	-23.264	-24.736

The FT cell count decreased most rapidly during the initial 6 hours followed by the slowest fall and yielded the highest (i.e. most stable) counts after about 20 hours till the end of the study.

The Real Room Temperature (RRT - 30°C to 40°C) counts exhibited the slowest fall in cell counts leading to highest counts among the treatment groups till 15 to 20 hours. After this period the rate of decrease in RRT counts did not change much till about 54 hours and then slowed down further and yielded the lowest count after about 45 hours among the treatment groups.

PT samples exhibited the most rapid drop in counts during the initial 25 hours and slowed down significantly after that. A rate of fall in PT cell counts, intermediate between FT and RT counts was seen during the initial 12 hours. PT counts were lowest between 10 to 40 hours as compared to other treatment groups.

The observation of highest significance was that for all the samples counterchecked repeatedly on automatic cell counter, the platelet counts showed the least variation from the initial count in contrast to the decreasing counts as observed with hemocytometry.

STATISTICAL ANALYSIS

The present study was a longitudinal, prospective study. The temperature of storage of blood samples was considered as a categorical variable. This type of study yields a longitudinal data set which cannot be subjected to “t-test” because observations were not equally spaced in time, cell lysis near the late stages of study yielded no values, hierarchical nature of the observations i.e. clustering (nesting) within subjects created a problem of serial correlations between observations and successive measurements in a subject were not independent of each other⁵⁻¹¹.

If time-by-time analysis had been opted for analysis it would have resulted in the inflated type I errors⁶

To obviate the problem of multiple comparisons and for the aforementioned problems with the dataset, summary measures method was used for analyzing the data from the study⁵⁻¹¹.

For comparing the rate of change of the platelet count among the three treatments, the summary measure adopted was the regression coefficient. And, for comparing the net absolute change in platelet counts among the groups, the summary measure chosen was the

time by which platelet counts decreased to 75 percent of the initial value (t_{75}) because after a drop of 25 percent in counts, it is reasonable to assume that the counts (i.e. the stored sample) were not fair enough representative of the original sample.

To evaluate the statistical significance among the study groups, a one-way repeated measures analysis of variance was performed over the t_{75} and regression coefficients.

The regression coefficients were derived by applying the Ordinary Least Square Regression (OLS regression) to the data points over the following initial hours: 35 hours for RRT, 25 hours for PT and 30 hours for FT.

The mean time by which platelet counts decreased to the 75 percent of the initial counts (t_{75}) were: RRT– 13 hours, PT– 5 hours and FT– 10 hours.

Planned contrast (simple) were obtained to compare mean t_{75} and regression coefficient for each of the three treatment conditions with the mean t_{75} and regression coefficient for the refrigerated samples (controls).

Mean t_{75} and mean regression coefficients during the RT and PT samples were significantly higher than baseline mean t_{75} . Thus, both RT and PT had significantly higher mean than the baseline conditions of 4°C storage.

DISCUSSION

A probable explanation of these variable patterns of decrease in platelet counts can be sought in the altered adhesive and disintegration characteristics of platelet under different storage conditions. These changes in platelet properties appear to be the consequences of platelet activation induced by the various mechanisms of platelet storage lesions, specially by the temperature at which the samples are stored and by adhesion with the glass of the hemocytometer. The development of platelet storage lesion is influenced by physical, chemical and metabolic factors related to platelet (or blood) withdrawal, preparation and storage.

Platelets show a contrasting behavior after storage at 4°C and 22°C. In general, the initial changes are more rapid (within 1 to 10 minute or initial a few hours) and more dramatic for 4°C storage consequent to drastic alterations in the platelet membrane dynamics. The lower metabolic rate at 4°C is the main factor responsible for

slower progression of the changes in comparison to the changes occurring at room temperature (20°C-24°C) storage¹²⁻¹⁵.

In contrast, the better preserved membrane integrity at 22°C accounts for slow developing initial changes. Whereas at 22°C, the higher metabolic rate leading to a greater fall in pH results in rapid development of cellular injury. These changes are consequent to the temperature-dependent alterations in platelet membrane dynamics that result in cytoskeletal reorganization and alterations in signal transduction and intracellular processes¹⁶⁻²³.

The works of Zhang²⁴, Vasin²⁵, Ruckenstein²⁶, James²⁷, Olef²⁸, and other studies mentioned previously concerned with platelet storage show that Platelets are least activated near 37°C. Platelet activation increases with decreasing temperature. At 4°C nearly all the platelets are activated. Even the room temperature (20° to 24°C) causes marked activation of platelets. The development of platelet storage lesions is much slower at 4°C than at 22°C.

At low temperatures, micro aggregate formation and increased viscosity of blood result in increased shear stress which changes ligand-receptor conformation to increase platelet adhesion^{18,27}. At high temperature, increased metabolic rate leads to a fall in pH²⁰.

When the temperature of storage is lowered, between 37°C to 30°C only subtle changes occur in platelet morphology. However, below 30°C clustering of lipid rafts of plasma membrane occurs due to liquid crystalline to gel phase transition, and is responsible for increasing platelet activation between 30°C and 20°C.^{18,24}

This increase in platelet activation subsequent to membrane lipid raft phase transition at 30°C manifests in increased platelet adhesion to glass which reflects in increased rate of fall in platelet counts in PT samples as compared to RT samples.

As the temperature is lowered further, most of the platelets are activated at 20°C. At 15° to 18°C the phospholipids of plasma membrane experience a liquid crystalline to gel phase transition^{18,24,29,30}. The cumulative effect of both the phase transitions greatly alters the membrane integrity, fluidity and membrane polarization and may account for the activation of nearly all the platelets at 4°C. Thus, this cumulative effect of temperature-graded differential membrane phase transition greatly increases platelet activation and

adhesion to glass to result in a very rapid drop in platelet counts during the first 6 hours in refrigerated (FT) samples.

The altered platelet membrane dynamics causes an increase in cytosolic calcium, cytoskeletal reorganization and altered cellular metabolism and ATP levels, which ultimately causes the lysis of platelets^{18,24,29,30,31}.

This way, increasing platelet activation with decreasing temperature and subsequent adhesion to glass surface appears to be the prime contributor to the platelet loss during initial hours (specially for refrigerated samples), whereas platelet disintegration plays a major role during later hours when activation is nearly complete^{28,32,33}.

These two phase of initial platelet adhesion to glass followed by their disintegration reflect as FT curves being mainly adhesive curves and the RT curves being predominantly the disintegration curves.

The most significant observation of the study was the discrepancy between cell counts from hemocytometer and automatic counter. It can be explained as follows:

As activated platelets undergo significant adhesion on glass, decreasing counts are recorded with hemocytometers, whereas for the samples counterchecked with automatic counters, the counts did not decrease because the blood is rapidly flushed through the instrument and consequently the platelets fail to adhere to the tubing of the cell counter. A basis of this adhesive behavior of platelets had been explored biophysically by Ruckenstein et al²⁶. The rate of sedimentation and adhesion of platelets onto a horizontal glass surface was studied by Ruckenstein et al.²⁶ They developed an equation for the rate of cellular deposition through a stagnant solution onto a horizontal surface for the case in which cells are transferred to the surface very rapidly compared with their rate of overcoming the potential barrier between them and the surface, The platelet adhesiveness, can be expressed in terms of the probability, $P = 1/\text{to overcome (i.e. escape over) the potential barrier between them and the surface}$, and is inversely proportional to the contact period during which appreciable deposition occurs, The time constant, depends exponentially on the potential barrier.

Vasin et al²⁵ developed a mathematical model of static platelet adhesion on a solid surface, taking the platelet activation in account. As shear stress decreased

the adhesion kinetic curves turned from exponential into sigmoid, as a result of accumulation of free activated cells in the surface vicinity. Platelet adhesion was also seen to be proportional to total activated platelet concentration.

The fall in platelet counts with time recorded with hemocytometers, at higher temperatures is mainly because of metabolic changes in platelets. The contribution of cell disintegration (fragmentation) to the decrease in counts may increase at higher temperatures and in older samples. In contrast, the fall in platelet counts, at lower temperatures is secondary to the dominance of platelet activation and the biophysico-chemical interactions in the (ionic) nanoenvironment, mediating the adhesion of activated platelets on glass surface^{34,35}.

These results indicate that even though the pathway for platelet activation is the same, the activation rate can be altered when specific interactions with the surface are involved. The results demonstrate the specificity in the way surfaces of materials activate platelets, depending on the platelet membrane dynamics and the intracellular calcium dynamics^{18,24,29,30,31,34,35}.

CONCLUSION

Thus it is concluded that: RT curves are predominantly the disintegration curves, whereas the FT curves are mainly adhesive curves.

The fall in platelet counts with time recorded with hemocytometers, at higher temperatures is mainly because of metabolic changes in platelets. The contribution of cell disintegration (fragmentation) to the decrease in counts may increase at higher temperatures and in older samples. In contrast, the fall in platelet counts, at lower temperatures is secondary to the dominance of platelet activation and the biophysico-chemical interactions in the (ionic) nanoenvironment, mediating the adhesion of activated platelets on glass surface.

These results indicate that even though the pathway for platelet activation is the same, the activation rate can be altered by the nanoenvironment based specific interactions of the surfaces with platelets. These interactions are the key modulators of the platelet membrane dynamics and the intracellular calcium dynamics, and thus they demonstrate the fine regulation of platelet activation secondary to the specificity of the surfaces – platelet interactions.

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ORIGINAL ARTICLE

Haematological Assessment of Petrol Pump Workers of Jaipur City

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ABSTRACT:

Background: Monitoring of occupationally exposed workers could be one of the important steps in evaluating risks and implementing strategies for improving occupational conditions in order to establish a safe working environment. With this perspective, this study was undertaken to find out the effect of gasoline vapors on the hematological parameters of the petrol pump filling attendants working at various petrol pumps of Jaipur city.

Material and methods: This study was conducted with 40 petrol pump workers working for more than three years at various petrol pumps of Jaipur city as study group and 40 matched male adults working as peons and ward boys in the different departments of the institute as the control group. Complete blood picture analysis was done using Automated 5 part Differential Cell Counter available at the Central Pathology Laboratory in S.M.S Hospital Jaipur. Mean \pm standard deviation values for each parameter were determined for both the study and control groups and compared using an unpaired *t*-test, and *P* < 0.05 was considered significant.

Result: The mean values of hemoglobin levels, total red blood cells (TRBC) and platelet count (PLT count) was significantly decreased in the petrol pump workers when compared to the control group. No significant differences were observed in differential leucocyte counts (DLC) between both the study and control group except the eosinophil count whose mean values were found highly significant in the petrol pump workers in comparison to the control group.

Conclusion: This preliminary study concludes that the petrol pump workers could be at greater risk to develop

hematological alterations with time. So, further long-term studies with large sample size and regular follow-ups are required to get better insights into the results.

Keywords: Gasoline vapors, Occupational exposure, Petrol pump workers, Complete blood count

INTRODUCTION

In recent decades, along with the economic growth, the level of urbanization in India has increased from 27.81% in 2001 to 31.16% in 2011¹. This substantial rise in the urban population throughout the country has led to many problems like increasing slums, poor sanitation and has also placed heavy demands on the urban transport systems and personalized vehicles^{2,3}. Consequently, mushrooming of petrol filling stations to gratify the increasing fuel needs of the expanding vehicular fleet⁴.

According to the Annual report entitled "Indian petroleum and natural gas statistics (2014-15)" brought by the Ministry of Petroleum and Natural gas, Government of India, New Delhi, the total petroleum retail outlets (petrol pumps) in India, has outgrown progressively from 36921 in 2008 to 53419 till march, 2015⁵.

These Indian Petrol pumps, alike many developing countries are manned by unskilled workers who dispense petrol/diesel without wearing any protective devices and many work for as long as 10-12 hours each day⁶. Thus, these fuel dispensers are continuously exposed to various gasoline derivatives like benzene, toluene, ethylbenzene, xylene in the form of vapors and tailpipe-emissions⁷.

The U.S National Institute for Occupational Safety and Health (NIOSH) considering BTEX as potentially hazardous to human health, stressed on the need to reduce

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its workplace exposure to the lowest feasible limit and suggested the recommended exposure limits (RELs) to be 0.1ppm ($0.319\text{mg}/\text{m}^3$), 100ppm ($375\text{mg}/\text{m}^3$), 100ppm($435\text{mg}/\text{m}^3$), and 100 ppm($435\text{mg}/\text{m}^3$), respectively for 8 hours-time weighted average (TWA)⁸. Also in India, Central Pollution Control Board (CPCB) has limited the benzene levels to be 5 micrograms per meter cube⁹.

However, a study conducted in Delhi by Sehgal et al from The Energy and Resources Institute (TERI) monitored benzene at 40 petroleum-filling stations in Delhi and within the breathing zone of the dispensing crew during 2009–2010 recognized an extremely high concentration of benzene, toluene and xylene at the filling stations with maximum observed values of 6406, 5890, and 9512 microgram per meter cube, respectively during winter months which was far exceeding than those laid down by the Indian national ambient air quality standards¹⁰.

An overseas study conducted in Italy showed that in a single refueling operation that lasts for about one minute, the mean air concentration of benzene to which a petrol pump worker is exposed is $3709\text{ }\mu\text{g}/\text{m}^3$, which indicates that the petrol pump workers are exposed to high concentrations of benzene in their breathing zone while fueling and re-fuelling of vehicles¹¹. Exposure to gasoline derivatives in form of vapors are not considered to be safe even inhaled for a brief period of time and owing to their occupation, the petrol pump workers are continuously exposed to such noxious chemical substances¹².

Thus, monitoring of such occupationally exposed workers could be one of the important steps in evaluating risks and implementing strategies for improving occupational conditions in order to establish a safe working environment.

Hence, this study was undertaken to find out the effect of gasoline vapors on the hematological parameters of the petrol pump filling attendants working at various petrol pumps of Jaipur city.

MATERIALS AND METHOD:

This study was undertaken at the Upgraded Department of Physiology in collaboration with the Central laboratory of the S.M.S Medical College, Jaipur after obtaining approval from the ethical committee of our institute and the written informed consent from the volunteers of the study.

A total of 80 subjects (40 petrol filling male attendants working for more than three years at various petrol pumps of Jaipur city and 40 matched controls from the institute working as peons and ward boys in the different departments) who met the selection criteria were included in the study. Subjects of both study and control group having a history of smoking, alcoholism, any acute or chronic illness, any major surgery (Cardiac, pulmonary, abdominal), any type of known allergic conditions, were excluded from the study. After, a brief physical, anthropometric (height, weight, body mass index [BMI]), and clinical examination, around 3ml of blood sample of each selected subject was collected in EDTA coated tube under aseptic precautions following the standard blood sampling protocols. Each EDTA coated tube containing the blood sample was labeled with a registration number issued for each subject by the computerized registration counter of the SMS hospital and was delivered within 2 hrs of the sample to the central laboratory of the Department of Pathology, SMS hospital, Jaipur for complete blood picture analysis using Automated 5 part Differential Cell Counter. All the tests were carried out during the morning OPD hours and the volunteers in the study were instructed for to avoid beverages such as tea, coffee, and other stimulants before reporting at the department for the tests.

Statistical Analysis :

Each parameter of complete blood counts of each subject was expressed as mean \pm standard deviation; statistical analysis was performed using unpaired Student's *t*-test and $P < 0.05$ was considered significant.

RESULTS

Table '1' observed that there was no statistically significant differences (p value > 0.05) was found in the means age, height, weight and BMI between study and control groups. The mean exposure years to gasoline in the study group (Petrol pump workers) were observed to be 9.78 ± 3.29 .

Table '2' depicted that all studied hematological parameters found to be decreased in study group than control group. This difference was statistically significant (p value < 0.05) in Hemoglobin, Total Red Blood Cell counts and Platelet counts but not in Total Leukocyte Count.

Table '3' depicted no significant differences (p value >0.05) between both the study and control group for neutrophil count, lymphocyte count and monocyte count however, the Mean \pm SD values for the eosinophil count were highly significant in the study group in comparison to the control group. Also, as the Mean \pm SD values for the

basophile count in the control group was observed (0.00 ± 0.00) so, the significance of difference in means for this hematological parameter between the petrol pump workers and the control group could not be calculated by the unpaired 't' test.

Table 1 : Characteristics Comparison of Subjects in Petrol Pump Workers and Control

Characteristics of Subjects		Mean \pm SD		p value	Significance
		Petrol pump workers (N=40)	Control Group (N=40)		
Anthropometric Parameters	Age (Yrs)	30.70 \pm 3.04	29.90 \pm 2.72	0.21	NS
	Height (Cms)	167.55 \pm 3.12	168.18 \pm 2.78	0.34	NS
	Weight (Kg)	61.70 \pm 3.95	63.25 \pm 4.89	0.12	NS
	BMI (Kg/M ²)	21.97 \pm 1.07	22.34 \pm 1.25	0.15	NS
Gasoline Exposure Years		9.78 \pm 3.29	-	-	-

NS: Not significant (p value >0.05)

Table 2 : Comparison of Hematological Parameters in Petrol Pump Workers and Control

Hematological Parameters	Mean \pm SD		p value	Significance
	Petrol pump workers (N=40)	Control Group (N=40)		
Hb (gm/dl)	13.89 \pm 0.90	14.69 \pm 0.59	<0.001	S
TLC(*1000/mm ³)	6.86 \pm 1.12	7.07 \pm 1.26	0.43	NS
TRBC (million/mm ³)	4.58 \pm 0.51	5.06 \pm 0.25	<0.001	S
Platelet count (Lakhs/mm ³)	2.01 \pm 0.47	2.54 \pm 0.53	<0.001	S

NS: Not significant (p value >0.05)

S=Significant (p value ≤ 0.05)

Table 3 : Comparison of Differential Leukocyte Counts in Petrol Pump Workers and Control

Various Types of WBC	Mean \pm SD		p value	Significance
	Petrol pump workers (N=40)	Control Group (N=40)		
Neutrophils (%)	54.47 \pm 6.20	56.40 \pm 6.61	0.18	NS
Lymphocytes (%)	34.82 \pm 5.78	34.68 \pm 6.28	0.92	NS
Monocytes (%)	6.53 \pm 2.23	6.13 \pm 2.57	0.45	NS
Eosinophils (%)	4.13 \pm 2.42	2.80 \pm 1.57	0.004	S
Basophils (%)	0.05 \pm 0.11	0.00 \pm 0.00	-	NC

NS : Not significant (p value >0.05), S=Significant (p value ≤ 0.05), NC= Not Calculated

DISCUSSION

In this study, some hematological investigations: complete blood counts were performed and compared between the petrol pump workers and the control subjects as these investigations are considered as good window to look into the general state of an individual's health.

It was observed that the mean values of hemoglobin levels were significantly decreased in the petrol pump workers when compared to the control group. By WHO criteria, anemia is defined as a hemoglobin concentration lower than 13 gm/dl in men¹³. In this study, 12.50 % of the petrol pump workers were found to be anemic.

Okoro et al (2006)¹⁴, Ali AA Shab (2011)¹⁵, T. Tunsaringkarn et al (2013)¹⁶ also reported a significant decline in the hemoglobin levels in petrol pump workers (exposed group) in comparison to the individuals who are not exposed to the workplace.

Additionally, the mean values of the total red blood cells (TRBC) and platelet counts (PLT count) were although within their respective reference ranges but were found significantly reduced in the exposed group, however, no significant differences were evident in the total leucocyte counts (TLC) between both the groups.

These findings were in accordance with the previous studies conducted by Anslem O Ajugwo et al (2014)¹⁷, which observed a significant decline in hematological indices (Hemoglobin levels, TRBC) in both the fuel filling attendants and auto-mechanics as compared to the control group. Hala Samir Abou-El Wafa et al (2015)¹⁸, Prosper Opute et al (2015)¹⁹ also reported a significant reduction in the formed elements of blood among the petrol pump workers.

As far as the results of differential leukocyte counts (DLC) were concerned, no significant differences were observed between both the study and control group for the neutrophil count, lymphocyte count and monocyte count, however, the mean values for the eosinophil count were found highly significant in the exposed group (Petrol pump workers) in comparison to the control group. Ray et al (2007)²⁰ also found a marked increase in the number of eosinophils and monocytes among such exposed workers.

In contrary to the hematological findings of this study, Tsai et al (2004)²¹ in a comparative study did not reveal any overt hemato-toxicity among the workers of petro-chemical industry. However, Lan et al (2004)²²

ascertained a significant reduction in the number of White Blood Cells and platelet counts among the workers occupationally exposed to benzene even below 1ppm. Qu et al (2002)²³ also observed a significant decrease in red blood cells, white blood cells and neutrophil counts in the benzene exposed workers.

According to Synder and Hedli (1996)²⁴ benzene toxicity involves both bone marrow depression and leukemogenesis caused by damage to multiple classes of hematopoietic cells and variety of haematopoietic cell functions. In milder forms of benzene toxicity individual cytopenias: anaemia, leucocytopenia and thrombocytopenia may occur.

This seems true to some extent in this study also as some of the petrol pump workers exhibited anemia, decrease in total red blood cell (TRBC) counts and platelet counts reflecting that with the prolonged exposure to the gasoline fumes, the fuel dispensers are more likely to develop the features of benzene toxicity.

The possible metabolic mechanisms for the underlying hematological alterations proposed by various investigators worldwide is that following inhalation, benzene and the other hydrocarbons present in gasoline are readily absorbed from the lungs and get metabolized in the liver by CYP450 2E1 oxidative pathways which lead to production of free radicals and quinone metabolites like phenol, hydroquinone, benzo-quinone, 1,2,4 benzenetriol. These free radicals and toxic metabolites cause lipid peroxidation and damage of hepatic cell membrane. The toxic metabolites like Phenol, catechol and hydroquinone are then transported in the bone marrow where these metabolites are further oxidized by myeloperoxidase (MPO) to benzoquinones and reactive oxygen species²⁵. Synder et al (1993) hypothesized that these benzene metabolites act together on early stem and progenitor cells, as well as on early blast cells, such as pronormoblasts and normoblasts and inhibit their maturation and amplification. Also, these metabolites inhibit the function of micro-environmental stromal cells necessary to support the growth of differentiating and maturing marrow cells²⁶.

Although, these peroxidase-mediated activation of phenolic metabolites of benzene which generates reactive quinones can be detoxified by NAD (P)H:quinone acceptor oxidoreductase (NQO1) and via conjugation with glutathione but many researchers believe that high

CYP2E1, MPO and low or negligible NQO1, GSTM1 and GSTT1 activities (high bio-activation with low detoxification) may be responsible for the increased risk of such benzene induced bone marrow toxicity^{27,28}.

However, despite of several lines of research, the precise mechanism so far remains inconclusive and still needed to be fully elucidated²⁸.

The limitation of this study was its small sample size, so it would be too early to generalize the results of this study to the entire population of petrol pump workers; however, the outcomes of such occupations become apparent after a number of years and thus, implication of strict rules and regulations, improvement in fuel quality and vehicle technologies, regular health checkups and providing safety devices to workers could be some early steps in prevention of long term morbidities^{18,29,30}.

CONCLUSION

This preliminary study concludes that the petrol pump workers could be at greater risk to develop hematological alterations with time. So, further long-term studies with large sample size and regular follow-ups are required to get better insights into the results.

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ORIGINAL ARTICLE

Clinical Profile of Stroke and Correlation of NIHSS, mRS with Special Reference to Homocysteine & Hypertension in a Tertiary Care Centre

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ABSTRACT

Introduction: Stroke is an important cause of disability and more than two thirds of survivors are left with disability. Stroke scales are used to assess severity of the disease as well as outcome of patient. This study aims to evaluate the clinical profile of stroke and relationship of hyper homocysteinemia, high systolic blood pressure (SBP) and diastolic blood pressure (DBP) with various stroke scales.

Materials and Methods: 102 patients of ischemic and hemorrhagic strokes were studied and National Institutes of Health Stroke Scale (NIHSS) and Intracerebral hemorrhage (ICH) scores on admission and Modified Rankin Score (mRS) at discharge and at 90 days were compared and relationship with serum homocysteine (Hcy) level in ischemic stroke and SBP & DBP in hemorrhagic and ischemic strokes were studied.

Results: The female: male ratio was 2:1 in ischemic and 1:1 in hemorrhagic stroke. Smoking, alcoholism, hyperlipidemia and diabetes were more common in ischemic stroke. NIHSS and mRS scores were higher in hemorrhagic stroke as compared to ischemic stroke. Patients with high NIHSS had high mRS score at discharge and at 90 days in ischemic and hemorrhagic strokes. This was also seen for ICH scores in hemorrhagic stroke patients. Higher homocysteine values were seen with higher NIHSS and mRS scores in ischemic strokes. Higher SBP and DBP were seen in higher NIHSS and mRS groups in both types of strokes.

Conclusions- Higher NIHSS and ICH score at admission were related with poor stroke outcomes. Higher homocysteine levels were related with poor

outcome in ischemic stroke. High SBP and DBP were seen with increased stroke severity and disability in both ischemic and hemorrhagic strokes.

Key words- DBP, Homocysteine, ICH score, mRS, NIHSS, SBP

INTRODUCTION

Stroke is an important cause of functional impairment and death all over the world. More than 65% of stroke survivors are left with a disability which impairs their ability to carry out activities of daily living unassisted. The stroke scale represents a useful tool for assessing the severity of a stroke attack and assessing the prognostic information of the hospital. Usually, the stroke scale is composed of several variables, used to observe symptoms and signs, and each variable is scored.

The National Institutes of Health Stroke Scale (NIHSS) is a fully validated and easy-to-implement stroke assessment score that is widely used worldwide. NIHSS is used to calculate all aspects of the nervous system examination and summarize the overall stroke damage. NIHSS has also been used to determine whether a patient is suitable for thrombolysis and predict the progression and outcome of acute stroke¹.

The next very common scale is the modified Rankin Scale (mRS). It is used as a measure of overall disability in stroke tests. It is easy to use, takes less time, has a wide validity period, and can also be taken over by telephone. The disadvantage is that the reliability is low, and an important part of incremental recovery may be missed².

In the case of hemorrhagic stroke, the severity can also be calculated from the ICH score. The ICH grading

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scale is a standard assessment tool, which can be easily and quickly determined in the performance of hemorrhagic stroke without any special neurological training. The various components of the scale (such as GCS, age, bleeding volume, intraventricular or lower abdominal position) are important predictors for predicting cerebral hemorrhage³.

Hyperhomocysteinemia is one of the modifiable risk factors of Ischemic stroke. It mainly depends on the serum levels of folic acid, vitamin B12 and vitamin B6^{4,5}. However, there are still few studies, and little is known about the relationship between Homocysteine (Hcy) levels and prognosis of stroke.

The relationship between post-stroke blood pressure (BP) and functional outcome in patients with acute ischemic stroke remains controversial. Although the results of observational studies have given conflicting results, high BP is associated with poor prognosis after acute stroke. Some authors even demonstrated better prognosis in patients with high initial BP⁶.

Therefore, the outcome assessment of stroke patients can be easily done with these scales, which can help in clinical decision-making, prognosis and patient recovery. These scores are rarely compared with each other. In addition, risk factors such as high serum homocysteine, and elevated DBP and SBP have rarely been studied in relation to stroke outcomes. With these things in mind, we conducted this research.

AIM OF STUDY

1. To correlate the significance of various stroke - related scale for prognostication of acute stroke.
2. To study effect of plasma homocysteine levels in ischemic stroke.
3. To study effect of systolic and diastolic blood pressure at presentation on acute stroke.

MATERIALS AND METHOD

The present prospective study was conducted in Department of Neurology at a leading Tertiary Care Medical College Teaching Hospital of North India.

Patients included in the study had a first-ever acute ischemic & hemorrhagic stroke diagnosed and treated in our department from October 2018 to September 2019. The diagnosis was made based on the clinical presentation and neuroimaging.

Informed consent was taken from each patient and

the study was approved by the ethical committee of the Institution.

Patients presenting with venous sinus thrombosis, subarachnoid hemorrhage, subdural hemorrhage, extradural hemorrhage, head injury or stroke mimickers like post ictal Todd's palsy etc were excluded from the study. Patients taking drugs that may affect homocysteine (such as oral contraceptives) or drugs that affect the metabolism of vitamin B12 or folic acid were also excluded.

A detailed medical history, including past medical history was recorded. A complete clinical and neurological examination including blood pressure check was performed. Blood pressure was measured in right arm supine position; both diastolic (DBP) and systolic blood pressure (SBP) were recorded. Each patient was evaluated by brain computed tomography (CT) within 24 hours after admission. Brain magnetic resonance imaging (MRI), CT angiography or MR angiography was performed in selected cases. Laboratory investigations and Serum homocysteine levels were done.

We calculated the NIHSS score of all patients on admission. NIHSS scores are divided into three groups, namely <8 (mild), 9-17 (moderate) and > 17 (severe). They were indicative of initial stroke severity. The ICH score for hemorrhagic stroke, including those with intraventricular extension was also calculated.

The early stroke outcome was measured at discharge using the modified Rankin scale (mRS). Most patients were discharged within a week of stroke onset and admission. We also calculated the mRS scores at day 90 after the onset, on outpatient basis or over telephone. mRS score were grouped into two components, namely (0-2) patients with independent prompt function and (3-5) patients with prompt function dependent.

Mean serum fasting homocysteine levels at admission were compared in different groups of stroke patients based on their NIHSS and mRS scores.

Based on the DBP and SBP on admission, ischemic and hemorrhagic patients were sub divided into three groups and mRS and NIHSS values of each group were compared against each other. SBP groups were ≤ 140 , 141 - 179 and ≥ 180 mmHg. DBP groups were ≤ 80 , 81 - 100 and > 100 mmHg.

Statistical methods:-

The collected data was coded, tabulated, and statistically analysed using IBM SPSS statistics (Statistical package for Social Sciences) software version 22.0.

The level of significance was taken at $p \text{ value} \leq 0.05$ as significant otherwise as non significant.

Correlation was denoted by Pearson's correlation coefficient.

Serum homocysteine levels were compared in different NIHSS and mRS score groups of ischemic stroke patients with corresponding p values.

NIHSS and mRS scores in previously mentioned 3 groups each of Systolic and Diastolic blood pressure were compared against each other and the level of significance was measured.

1. Demographic Profile (n=102):

Parameter		Hemorrhagic	Ischemic
Total number		24	78
Gender	Male	12	28
	Female	12	50
Age	Age(M)(in yrs)	54.5 \pm 14.8	59.6 \pm 13.9
	Age(F)(in yrs)	60 \pm 12.8	62.3 \pm 9.3
Risk Factors	Smoking	8	46
	Alcohol	1	10
	Diabetes	1	14
	Hypertension	13	12
	Hyperlipidemia	0	10

Among 102 stroke patients, 24 were hemorrhagic strokes, and the remaining 78 were ischemic strokes, of which 64 were thrombotic (T) and 14 were embolic (E). There were 12 males and 12 females in the hemorrhagic stroke group; 28 males and 50 females in the ischemic stroke group. The average age of men and women in the hemorrhagic stroke group was 54.5 and 60 years old, respectively and the average age of the ischemic stroke group was 59.6 years and 62.3 years for men and women,

respectively. There were 8 smokers in the hemorrhagic group and 46 in the ischemic group. The corresponding numbers for alcoholics were 1 and 10 respectively. There was 1 case of diabetes in hemorrhagic group, and 14 cases in the ischemic stroke group. 13 patients in hemorrhagic and 12 patients in ischemic were previously known hypertensive. Only 10 patients had previously reported hyperlipidemia in ischemic group, no cases of known hyperlipidemia was reported by hemorrhagic group.

2. Distribution of various stroke-related scales (NIHSS, mRS at discharge & at day 90) in Hemorrhagic stroke(n=24)

Parameter	NIHSS scores			mRS scores (at discharge)		mRS scores (at day 90)	
	<8	8-16	≥ 17	0-2	3-5	0-2	3-5
	4	7	13	6	18	13	11
Mean Value	15.79 \pm 6.15			3.2 \pm 1.19		2.4 \pm 1.4	

In patients with hemorrhagic stroke, the NIHSS score of mild severity (<8) is 16.66%, moderate severity (8-16) is 29.17%, and severity (>17) is 54.17%. The average NIHSS score of patients with hemorrhagic stroke was 15.79 ± 6.15 .

The mRS scores indicating independent functioning at time of discharge of (0-2) was seen in 25% of patients and functional dependence (3-5) was seen in 75% of patients. While on follow up at day 90,

independent functioning (0-2) was seen in 54.2% and dependency (3-5) was seen in 45.8%. Mean of mRS scores at time of discharge and on day 90 was 3.2 ± 1.19 and 2.4 ± 1.4 respectively.

On comparing NIHSS vs mRS scores of hemorrhagic patient, there was a significant relationship between NIHSS on admission with mRS at discharge (p Value=0.026) and mRs at 90 days follow up (p Value= 0.001).

3. Distribution of various stroke-related scales (NIHSS, mRS at discharge & at day 90) in Ischemic stroke (n=78)

Parameter	NIHSS scores			mRS scores (at discharge)		mRS scores (at day 90)	
	<8	8-16	≥ 17	0-2	3-5	0-2	3-5
	20	33	25	38	40	60	18
Mean Value	12.96 ± 6.81			2.7 ± 1.33		1.7 ± 1.38	

In patients with ischemic stroke, NIHSS scores of mild severity (<8) was seen in 25.64%, moderate severity (8-16) in 42.30% and greater severity (≥ 17) in 32.05%. Mean of NIHSS score was 12.96 ± 6.81 .

The mRS scores indicating independent functioning at time of discharge of (0-2) was seen in 48.7% of patients and functional dependence (3-5) was seen in 51.3% of patients. While on follow up at day 90, independent functioning (0-2) was seen in 76.9 % and dependency (3-5) was seen in 23.07 %. Mean of mRS scores at time of discharge and on day 90 was 2.7 ± 1.33 and 1.7 ± 1.38 respectively.

On comparing NIHSS vs mRS scores of ischemic patient, there was a significant relationship between NIHSS on admission with mRS at discharge (p Value- 0.065) and that on 90 days follow up (p Value- 0.005).

There was a significant positive correlation between NIHSS vs. ICH scores on admission in hemorrhagic patients and also between mRS at time of discharge and ICH score on admission in these patients.

4. Correlation between ICH score vs. NIHSS score and ICH score vs. mRS score at time of discharge in hemorrhagic stroke patients

NIHSS Score	0-8	9- 16	17 and above
ICH Score(Mean)	1 ± 1	1.57 ± 1.27	2.36 ± 0.74
mRS Score	0-2		3- 5
ICH Score(Mean)	0.9 ± 0.99		2 ± 1.03
	NIHSS vs ICH score on admission		mRSvs ICH score
Pearson correlation	0.685		0.571
P value	0.000		0.004

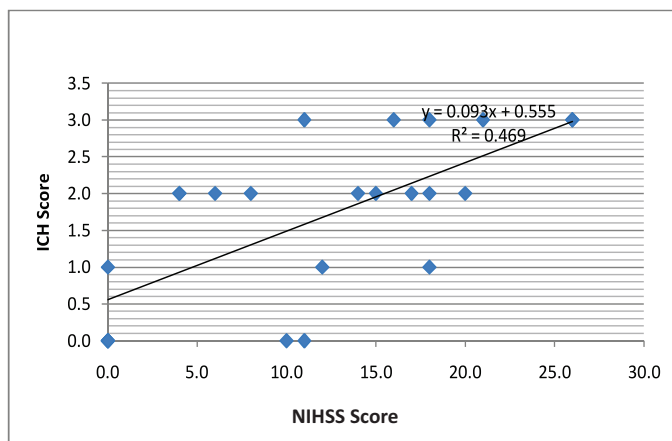


Figure 1: Correlations of ICH Score with NIHSS Score

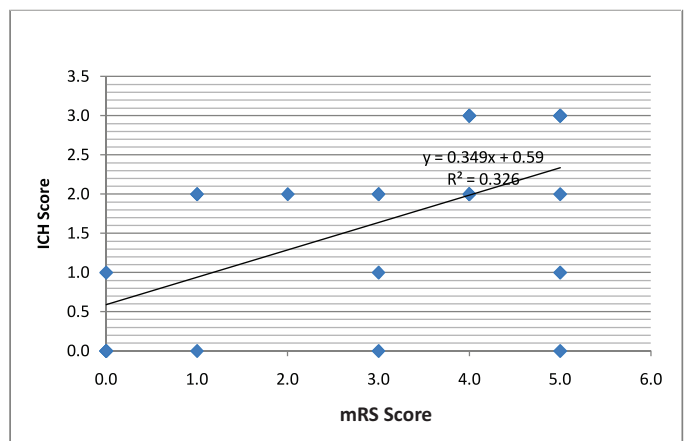


Figure 2: Correlations of ICH Score with mRS Score

5. Comparison between mean serum Homocysteine levels in different mRS and NIHSS score groups of ischemic stroke patients

	mRS scores		NIHSS scores		
	0-2	3- 5	<8	8- 17	≥17
No. of patients	38	40	20	33	25
S.Homocysteine (mean)	21 ±10.3	32.35±11.92	19.44±7.44	24.77±13.66	36.15 ±
P value	<0.001		<0.001		

On comparing the serum homocysteine values at admission in different mRS and NIHSS score groups, the difference was found to be significant.

6. Comparison of NIHSS score on admission and mRS scores at 90 days in 3 different SBP groups (in mmHG) in Ischemic stroke patients

		No. of Patients (n=78)	Mean NIHSS Score	Mean mRS Score	P value	
					NIHSS	mRS
SBP (mm Hg)	≤140	23	8.8±4.85	1.90±0.81	<0.001	0.01
	141-179	25	11.56±7.34	2.4±1.12		
	≥180	30	17.48±6.62	3.53±1.32		
DBP (mm Hg)	≤80	20	6.6±3.22	1.55±0.69	<0.001	<0.001
	81- 100	27	11.7 ±5.18	2.22±0.85		
	>100	31	17.8±5.93	3.79±1.11		

On comparison of NIHSS and mRS scores in 3 different groups each of SBP and DBP in ischemic stroke

patients taken at admission, the difference in the NIHSS and mRS scores of different groups of SBP and DBP was significant.

7. Comparison of NIHSS on admission with mRS at 90 days groups(in mmHg) in Hemorrhagic stroke patients

		No. of pts (n=24)	Mean NIHSS	Mean mRS	P value	
					NIHSS	mRS
SBP (mm Hg)	≤140	5	10.2±7.22	2±1	0.008	0.002
	141- 179	8	14.8±6.84	3.12±1.36		
	≥180	11	19.1±2.95	3.81±0.75		
DBP (mm Hg)	≤80	4	10.25±6.13	2.0±0.82	0.04	0.01
	81-100	11	15.82±7.77	3.18±1.32		
	>100	9	18.22±1.39	3.78±0.83		

On comparison of NIHSS and mRS scores in 3 different groups each of SBP and DBP taken at admission in hemorrhagic stroke patients, the difference in the NIHSS and mRS scores of different groups of SBP and DBP was significant.

DISCUSSION

We wanted to find whether severe strokes at presentation had poorer outcomes and whether high blood pressure and homocysteine levels could be predictive of stroke outcomes. Ischemic strokes constituted 76.47 percent of patients and rest were hemorrhagic strokes. Another Iranian study⁷ found that 84.3% strokes were ischemic and rest were hemorrhagic strokes. Such differences in numbers could be attributed to regional variations and other variables like illiteracy, belief on faith healers, etc seen in this part of the world. This difference could be accounted for a higher incidence of hemorrhagic stroke in the Indian community than in the Western countries⁸.

Sex preponderance was seen in ischemic strokes female (2:1), while sex distribution was equal in hemorrhagic strokes, similar to the observations by Aiyar et al⁹. Sylaja et al⁸, in their seminal research, had only one third of stroke patients who were females. In our study, stroke onset occurred at an older age in women as compared with men. The mean ages of stroke onset were 60 yrs and 54.5 yrs for hemorrhagic and 62.3 yrs and 59.6 yrs in ischemic stroke in females and males respectively. Riley et al¹⁰, noted that this age variation could be due to a fall in sex hormones around menopause. Ong et al had similar observations with regard to age of stroke patients¹¹. However, the mean age for females was 72.18 years vs. 60.95 yrs as we found and for males this was 68.29 yrs vs. 68 yrs, respectively. Therefore, we saw a younger age at onset of stroke in females while the values for males were similar. In our study, 82% of ischemic strokes were thrombotic in type and others were embolic. In a review by Banerjee et al¹², 59% of ischemic strokes were thrombotic, and 10 % were cardioembolic, 4% were on account of causes like vasculitis while 27% were of undetermined origin. More detailed workup was restricted due to financial considerations; this could have better elucidated the causes.

Coming to the risk factors, we found a higher preponderance of smokers, alcoholics and diabetics in ischemic stroke patients amongst which 58.9% of

ischemic stroke patients were smokers. As compared to western population, Indians had a higher rate of tobacco and alcohol use according to Sylaja et al⁸.

Based on NIHSS scores at admission, 21.79% of ischemic and 16.66% hemorrhagic patients had mild, 47.43% ischemic and 16.66% of hemorrhagic cases had moderate and rest were more severe strokes. In a study by Bhaskar et al¹, the distribution for mild, moderate and severe NIHSS scores for ischemic stroke were 31.6%, 34.6% and 33.8%, respectively. Thus we had larger proportion of moderate and severe strokes. The NIHSS groups in intracerebral bleed patients as found by Mohammed et al¹¹, were mild to moderate severity in 46% and rest were more severe, a finding similar to our observations. The mean NIHSS scores of hemorrhagic patients was 15.79 ± 6.15 , while in ischemic patients this was 12.96 ± 6.81 implicating a greater severity of hemorrhagic stroke as compared to ischemic.

On comparing mRS values in ischemic stroke, 48.7% were independent and 51.3% were dependent in our study at discharge while these values were 76.9% and 23.07% at 90 days, respectively. At discharge, only one third of hemorrhagic patients were independent while rest were dependent and these values improved to 54% independent and rest dependent, at 90 days follow up. In a study by Rodriguez et al, mRS at 90 days was 50% in ischemic stroke patients⁹, which was almost similar to our study. In the same study they found that 40% of hemorrhagic patients were functionally independent and rest were either dependent or dead. The mean mRS scores in our hemorrhagic stroke patients was higher than ischemic patients, again indicating poorer functional outcomes in hemorrhagic patients.

On comparing the influence of initial stroke severity with patient outcomes at discharge and at 90 days, in ischemic and hemorrhagic stroke patients, there was a significant association meaning that more severe strokes had poorer functional outcomes. In an article published in the Stroke journal, it was stated that acute impairment score (NIHSS) independently predicted mRS at 2 months to 1 year post stroke¹². Bhaskar et al¹ also found that initial stroke severity had a dominant impact on stroke outcome at 90 days.

Mahdy et al¹³ found a significant positive correlation between mRS score and ICH score similar to what we found in our study. They also found that the intra

cerebral hematoma volume on admission had a significant positive correlation with the NIHSS. Standing by this, we also got higher stroke severity in those with higher ICH scores. Combining these two results, ICH score can well be used to prognosticate hemorrhagic strokes.

Raised serum homocysteine was associated with higher NIHSS and mRS scores in our study. Biswas et al¹⁴, observed that homocysteine levels are higher in a stroke population. Bonthapally et al also found that homocysteine level correlated well with severity of disease assessed by NIHSS¹⁵. Acute phase elevated homocysteine correlated with severity and prognosis in patients with atherothrombotic stroke as noted by Xu Qing Wu et al¹⁶. This was also observed by Kwon et al¹⁷ that there was a significant positive correlation between homocysteine values on admission and NIHSS at 7 days and mRS at 90 days.

Patients who had higher systolic blood pressure at presentation also had higher NIHSS and mRS scores in both ischemic and hemorrhagic stroke groups. Similar findings with regards to diastolic blood pressure groups were observed in above patient groups. In a systematic review by Wilmot et al¹⁸, high systolic blood pressure, mean arterial blood pressure and diastolic blood pressure in the acute phase of stroke are associated with a poor outcome as death or as combined death or disability and combined death or early deterioration as assessed by the NIHSS and mRS and other stroke scales. Soliman et al¹⁹ similarly observed that NIHSS and mRS scores were significantly higher in hypertensive patients with acute ischemic stroke. Thus, initial blood pressures can have a significant impact on stroke severity outcomes.

CONCLUSIONS

1. Higher NIHSS scores on admission were suggestive of higher ICH scores (in hemorrhagic stroke) as well as higher mRS scores at 3 months follow up in patients of ischemic or hemorrhagic stroke.

2. Serum homocysteine levels on admission were significantly higher in ischemic stroke patients with higher NIHSS scores and mRS at 3 months.

3. Higher systolic and diastolic blood pressures at presentation were related to higher NIHSS and mRS scores.

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REVIEW ARTICLE

Covid 19: A Review of Existing Literature

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BACKGROUND

On the doorstep of 2020, 44 cases of pneumonia of unknown etiology were reported within 4 days in Hubei province of Wuhan city of China. Chinese authorities identified a new type of Coronavirus first on 7 January 2020 and the outbreak was associated with exposures in one seafood market in Wuhan city. First laboratory confirmed case of SARS-CoV-2 (previously named 2019-nCoV) outside China was reported in Thailand with travel history to Wuhan, China on 13 January. Japan reported a case of SARS-CoV-2 on 15 January. South Korea reported similar case with history of travel from Wuhan on 20th Jan 2020¹.

In the span of 1 month, 20 countries were affected with having total 9826 confirmed cases worldwide including 9720 cases in China and 106 cases in other 19 countries. WHO declared the outbreak to be a public health emergency of international concern on 30 January and was declared as a Global Pandemic on 11 March 2020². India reported first confirmed case on 30 January in Kerala with travel history from Wuhan³.

As of Jan 10, 2021 data shows 8,83,87,352 cases globally with case fatality rate of 2.17% with a total of 19,19,204 deaths⁴. In Europe, the total numbers of cases were reported to be 28 797 583 with case fatality rate of 2.1%. USA is worst hit country and with 3,88,61,668 cases. India has second highest number of cases (1,04,50,284) with case fatality rate of 1.44%⁴. In India, the worst hit state is Maharashtra.

VIRUS STRUCTURE, INFECTION AND PATHOPHYSIOLOGY

Coronaviridae are enveloped positive sense single stranded RNA viruses of 30kb. Among the 4 genera of alpha, beta, gamma, delta, alpha and beta coronaviruses

infect mammals. SARS-CoV, Middle East Respiratory Syndrome virus and SARS-CoV2 belong to beta coronaviridae⁵.

Surface projections- a structural protein called spike is composed of transmembrane trimetric glycoprotein protruding from viral surface, which determines the diversity of coronavirus and host tropism. Angiotensin converting enzyme (ACE-2) is a functional receptor for SARS-CoV; however, high ACE2 was highly expressed in lung, heart, ileum, kidney and bladder. Spike comprises of two functional subunits; S1 subunit binds to host cell receptor and S2 subunit is for fusion of viral and cellular membranes. The coronavirus spike is unusual among viruses because a range of protease can cleave and activate it. Unique to SARS-CoV-2 is the existence of "Furin" cleavage site (RPPA sequence) at S1/S2 site, which makes the virus extremely pathogenic. Immune mediated inflammation plays a pivotal role in secondary viremia. Severity is associated with progressive lymphopenia and neutrophilia. Reports are also suggestive of reduced lymphocyte count, elevated ferritin, IL-6 and D-Dimer were associated with increased mortality. Cytotoxic lymphocytes such as cytotoxic T lymphocytes (CTLs) and natural killer (NK) cells are necessary for the control of viral infection; however, functional exhaustion of cytotoxic lymphocytes is correlated with disease progression⁶.

Cytokine storm: Evidence suggests the role of multiple proinflammatory cytokines, including IL-6, IL-10, G-CSF, Monocyte chemotactic protein 1. Macrophage inflammatory protein 1 (MIP1) alpha TNF and CRP⁷.

Hypercoagulability and thrombus formation: SARS-CoV-2 causes endothelial injury to pulmonary

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vasculature⁸ that plays a central role in pathogenesis of ARDS and multiorgan failure. Vascular changes include diffuse alveolar damage and formation of fibrin thrombi. The lungs from patients with covid-19 had significant new vessel growth through a mechanism of intussusceptive angiogenesis⁹. Evidence suggests increase in factor VIII, fibrinogen, circulating prothrombotic microparticles, neutrophil extracellular traps (NETs) and hyperviscosity causes hypercoagulable state in turn leading to Diffuse Intravascular Coagulation (DIC) leading to ARDS and multiorgan failure¹⁰.

CLINICAL CHARACTERISTICS

COVID-19 primarily spreads through the respiratory tract, by droplets, respiratory secretions, and direct contact. Respiratory illness can range from a mild respiratory infection to a life threatening pneumonia and ARDS. Majority of SARS-CoV-2 infected individuals (80%) are asymptomatic or present mild symptoms¹¹. On the other end, symptomatic individuals may evolve to more severe symptoms and even death. 1099 laboratory-confirmed cases, found that the common clinical manifestations included fever (88.7%), cough (67.8%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), and headache (13.6%)¹². Among hospitalized patients with COVID-19 complications such as pneumonia, sepsis, respiratory failure, and acute respiratory distress syndrome (ARD) are frequently found¹³. Although observational studies reported older age and the presence of comorbidities as risk factors for increased disease severity in patients with COVID-19, it rapidly became clear that severe disease can also occur in younger patients with no pre-existing medical conditions¹⁴.

DETECTION METHODS:

Nucleic acid detection

Nucleic acid detection technology has the characteristics of early diagnosis, high sensitivity and specificity. 'Diagnosis and Treatment Guideline of the Novel Coronavirus Pneumonia' of China proposed to use fluorescent-tagged probe based real-time RT-PCR to detect SARS-CoV-2 nucleic acid in respiratory specimens or blood specimens¹⁵.

Antibody detection

Many serological tests for covid-19 have become available in a short period as they might be cheaper and

easy to implement at point of care. A recent systematic review and meta-analysis assessed the diagnostic accuracy of serological tests for SARS-CoV-2 infection¹⁶. Sensitivity was higher at least three weeks after symptom onset (ranging from 69.9% to 98.9%) compared with within the first week (from 13.4% to 50.3%). This means of those tested for covid-19 within one week of symptom onset, on average 44% to 87% will be falsely identified as not having infection. Thus current serological tests for covid-19 have limited utility in the diagnosis of acute covid-19.

PREVENTION:

To date, no effective vaccination is available. The risk of acquiring secondary and atypical infections is more so in cases of immune compromised individuals. Therefore, the best way in order to protect oneself is to follow the conventional infection control protocols and avoid unnecessary travel, public transport, contact with sick people and so on.

Appropriate use of face mask

N95 is a good fit mask preventing the entry of droplets and thereby minimizing the chance of acquiring the infection.

Decontamination of N95 respirators

- Ultraviolet light
- Hydrogen peroxide vapor - The U.S FDA has granted an emergency use authorization for use of low temperature vaporous hydrogen peroxide sterilizers, used for medical instruments to decontaminate N95 respirators¹⁷.
- Moist heat - Moist heat was applied by preparing a container with one liter tap water in bottom and dry horizontal rack above water, container was sealed and warmed in an oven to 65 degree Celsius for atleast 3 hours and then opened, the respirator placed on the rack, and the container resealed and placed back in oven for additional thirty minutes¹⁸.

CURRENT THERAPEUTIC TREATMENT

DRUG EVOLUTION

Given the lack of effective antiviral therapy against SARS-Cov-2, current treatments are mainly focused on symptomatic relief and respiratory support. Finding drugs that can bind to the viral protein and stop them from working is a logical way forward. The laborious, decade

long, classic pathway for the discovery and approval of new drugs could be less suited to the present pandemic. Repurposing existing drugs offers a potentially rapid mechanism to finding cures for unforeseen diseases, since the pharmacokinetics and safety profiles are known.

ANTIVIRALS-

Hydroxychloroquine

- It has several antiviral properties including inhibition of inflammatory cytokines such as IL-1, IL-6 and TNF- α .
- It also inhibits SARS-CoV-2 entry by changing the glycosylation of ACE2 receptor and spike protein.
- HCQ can block the endosome maturation at intermediate stages of endocytosis, resulting in failure of virion transport to releasing site.

While initial evidence pointed towards efficacy of hydroxychloroquine in decreasing the clinical severity of disease and prophylaxis, later evidence has found limited role of HCQ does not result in reduction of mortality of hospitalized patients. A recent systematic review was conducted with the objectives of evaluation of safety and efficacy of HCQ. It included seven studies ($n=1358$) and no difference was observed in virological cure (OR, 2.37, 95% CI, 0.13-44.53), death or clinical worsening of disease (OR, 1.37, 95% CI, 1.37-21.97), and safety (OR, 2.19, 95% CI, 0.59-8.18), when compared with the control/conventional treatment¹⁹.

Remdesivir

Remdesivir exhibits broad-spectrum antiviral activity against RNA viruses like Ebola virus (EBOV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Remdesivir has been reported to inhibit viral RNA synthesis by a specific mechanism of delayed chain termination²⁰. It has been used in the dose of 200 mg administered intravenously on day 1, ensued by 100 mg daily for the remaining days for a total of 5-10 days.

Contraindications:

- AST/ALT > 5 times Upper limit of normal (ULN)
- Severe renal impairment (i.e., eGFR < 30ml/min/m² or need for hemodialysis)
- Pregnancy or lactating females
- Children (< 12 years of age)

Lopinavir+Ritonavir

Lopinavir and ritonavir are protease inhibitors which

disrupt the process of viral replication and release from host cells while ritonavir additionally inhibits enzyme cytochrome P450 3A and therefore increases the half-life of lopinavir. Based on currently available data, there is no clear benefit for the use of lopinavir-ritonavir compared to standard of care in severe COVID-19²¹.

Favipiravir

Favipiravir acts by inhibition of RNA-dependent RNA polymerase enzyme which is used in transcription and replication of the viral genome.

In an open-label non-randomized control study conducted by Q Cai et al, favipiravir (FPV) 1600 mg twice daily as a loading dose and 600 mg twice daily plus interferon (IFN)- α 5 million U twice daily by aerosol inhalation were administered to 35 patients with a median age of 43 (35.5–59) years²². They observed a shorter viral clearance time and significant improvement in chest imaging in FPV group with few adverse reactions. Currently there are 32 clinical trials under various phases of development for the use of favipiravir for COVID-19²³.

IMMUNOMODULATORY AGENTS

Cytokine storm has been associated with severity of disease. Studies have also shown that expression of IL-2R and IL-6 in serum appears to predict the severity and prognosis. Hence, combined treatment of an immunomodulatory agent to reduce the cytokine storm along with an antiviral agent may show promising results. Elevated levels IL-6 is a predictor of worst outcome in patients with covid-19.

A. Tocilizumab

Monoclonal antibody against IL-6 blocks the signal transduction and has been considered in patients with elevated levels of IL-6.

Tocilizumab (Off Label) may be considered in patients with moderate disease with progressively increasing oxygen requirements and in mechanically ventilated patients not improving despite use of steroids. Long term safety data in COVID 19 remains largely unknown. It is administered in the dose of 8mg/kg (maximum 800 mg at one time) given slowly in 100 ml normal saline over 1 hour; dose can be repeated once after 12 to 24 hours if needed²⁴.

Special considerations before its use include:

- Presence of raised inflammatory markers (e.g., CRP, Ferritin, IL-6)

- Patients should be carefully monitored post Tocilizumab for secondary infections and neutropenia.
- Active infections and Tuberculosis should be ruled out before use.

B. Interferon-beta (IFN-beta)

Interferons modulate both T-and B-lymphocyte responses by promoting the proliferation of memory T-cells, stimulating the differentiation of Th1 cells, inducing IFN- γ secretion from T-cells, and promoting isotype switching in B cells and differentiation into plasma cells.

They have widespread potential as therapeutic agents for viral infections. IFNs inhibit viral infection by preventing viral entry into target cells and by blocking different stages of the viral replication cycle for different viruses.

A prospective non controlled trial done by Farzaneh Dastan²⁵ et al showed resolution of fever within first 7 days in all patients and significant decrease within 10 days and recovery in imaging study after 14 days in all patients.

An open label randomized phase 2 trial conducted by Ivan Fan-Ngai Hung et al concluded that early triple antiviral therapy was safe and superior to lopinavir–ritonavir alone in alleviating symptoms and shortening the duration of viral shedding and hospital stay in patients with mild to moderate COVID-19²⁶. Future clinical study of a double antiviral therapy with interferon beta-1b as a backbone is warranted.

C. Low dose steroids

Glucocorticoids may modulate inflammation-mediated lung injury in Covid-19 and thereby reduce progression to respiratory failure and death. The preliminary results of the controlled, open-label Randomized Evaluation of Covid-19 Therapy (RECOVERY) trial²⁷ of dexamethasone in patients hospitalized with Covid-19 provide evidence that treatment with dexamethasone at a dose of 6mg daily for up to 10 days reduces 28-day mortality among those who are receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support.

An interventional randomized clinical trial²⁸ comparing High Versus Low Dose Dexamethasone for the treatment of COVID-19 Related ARDS is currently under phase 3.

ANTITHROMBOTIC THERAPY

Low molecular weight heparin (LMWH)

As evident in a meta-analysis of four published

studies, derangement of coagulation parameters has been found to be common in patients with severe form of COVID-19 infection and associated with a poor prognosis²⁹. In these patients, low molecular weight heparin (LMWH) or unfractionated heparin (UFH) at doses registered for prevention of venous thromboembolism (VTE) seemed to be associated with a lower risk of death³⁰ and is currently recommended by the World Health Organization³¹.

CONVALESCENT PLASMA TRANSFUSION

Immune (i.e. “convalescent”) plasma refers to plasma that is collected from individuals following resolution of infection and development of antibodies. Passive antibody administration through transfusion of convalescent plasma may confer immediate immunity to susceptible individuals. Evidence shows that convalescent plasma from patients who have recovered from viral infections can be used as a treatment without the occurrence of severe adverse events³².

OXYGEN THERAPY AND RESPIRATORY SUPPORT

Respiratory failure is the primary organ dysfunction, which worsens the prognosis of COVID-19 patients. Oxygen therapy and respiratory support are the key treatments for COVID-19-induced ARDS. Hypoxemia is the hallmark of the pulmonary derangement of the disease, in fact a case series of COVID-19 patients demonstrated the presence of significant hypoxemia with no signs of respiratory distress (“*silent hypoxemia*”)³³.

For spontaneously breathing patients with mild-to-moderate dyspnea and hypoxemia, non-responsive to regular low-flow nasal cannula, initial approach may involve the use of high flow nasal cannula (HFNC) and awake prone positioning based on limited clinical data. HFNC, although initially controversial due to its aerosolizing potential, it was found to be safe in further studies, with a bio-aerosol dispersion not significantly different from regular nasal prongs³⁴.

NIV support (continuous positive airway pressure [CPAP] or Bi-level positive airway pressure [BiPAP]) has been employed in COVID-19 patients as a last resource to circumvent endotracheal intubation after failing HFNC and awake prone positioning, although no formal recommendation regarding their use has been released.

For COVID-19, there is no sufficient evidence to prove that HFNC is superior to NIV.

It is paramount to closely monitor the respiratory efforts in COVID-19 patients spontaneously breathing (regardless of the use of HFNC or NIV support). Institution of endotracheal intubation and mechanical ventilation should be made as soon as possible regardless of the phenotype of the COVID-19 pneumonia, when signs of respiratory distress are associated to the severe hypoxemia³⁵.

Prone positioning has been advocated in intubated patients with Covid-19 associated ARDS (CARDS). Pan et al. demonstrated increased lung recruitability and PaO₂/FiO₂ improvement after prone positioning in patients with moderate CARDS³⁶. Prone positioning leads to a relieve of severe hypoxemia due to reduction of overinflated lung areas, promoting of alveolar recruitment and decreasing ventilation/perfusion mismatch.

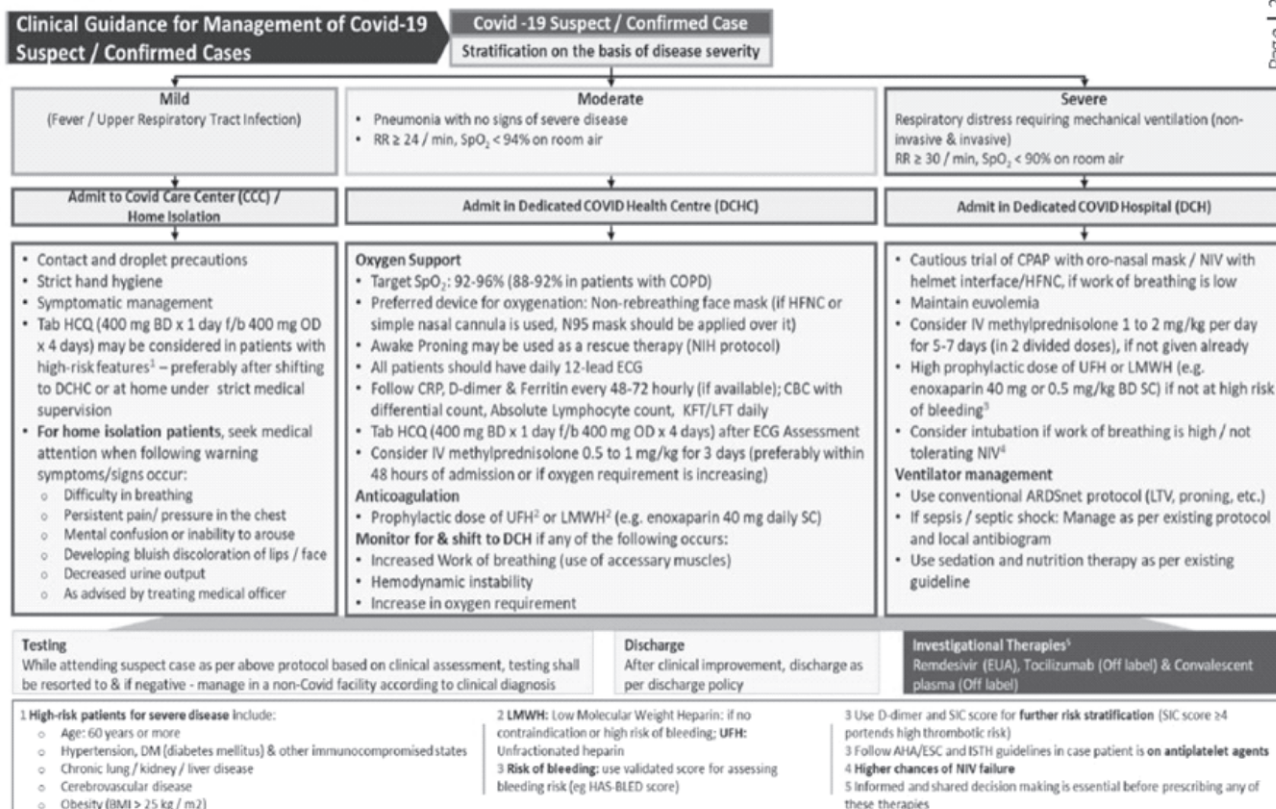
CONCLUSION

The current COVID-19 pandemic has become an international public health problem. There have been rapid advances in what we know about the virus, its transmission and how it causes illness and clinical characteristics and management of COVID-19. Currently, a vaccine is not available, neither is a specific antiviral treatment. Early identification of suspect cases, isolation, infection control, and providing symptomatic care are vital for overcoming the pandemic.

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CASE REPORT

Mucoepidermoid Carcinoma of Lung– A Rare Case with Unusual Presentation

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ABSTRACT

Mucoepidermoid carcinoma of the lung (MEC) is a rare entity. We present a case of a 36-year-old non-smoker female who presented with cough, fever and left sided chest pain for the past 6 months. Chest X ray revealed as trapped lung and CT demonstrated a left bronchial mass. On CT guided bronchial biopsy, it was diagnosed as squamous cell carcinoma. Diagnosis of MEC was made on pneumonectomy specimen received. The histological grade affects the progression and survival. Although metastasis is rare but it can occur.

Keywords: Mucoepidermoid, lung, carcinoma, rare

INTRODUCTION

Salivary gland type tumours are the unusual family of the primary neoplasms of the lung, the histology of which recapitulates neoplasm of the salivary gland. In general, primary salivary gland tumour of the lungs are rare¹. Mucoepidermoid carcinoma is common among these rare salivary gland tumours. It can affect males and females across a broad age range, including children and usually present as an exophytic endobronchial mass. These tumours mostly originate from the sub mucosal glands of the bronchi and clinically patient presents with symptoms of bronchial obstruction such as cough, wheezing or atelectasis². They are comprised of cells showing epidermoid differentiation admixed with mucocytes containing mucin¹. Based on the World Health Organization (WHO) classification these are further sub classified into low grade and high grade with low grade having a good clinical outcome when completely rejected while mucoepidermoid carcinoma with high grade histology show highly aggressive behaviour. Diagnosis

relies on the histopathological examination of the biopsy since the clinical and radiological manifestations are not specific³. Epidermal Growth Factor Receptor (EGFR) is frequently over expressed in MEC's. Pulmonary MEC's may harbour at (11;19) translocation with an associated novel fusion oncogene (CRCT1-MAML2)⁴.

CASE PRESENTATION

A 36-year-old female, non-smoker presented with cough without expectoration, fever and left sided chest pain for 6 months. CT of the chest showed mildly reduced left lung volume with focal area of collapse consolidation in the posterior segment of left lower lobe and near complete obstruction of the lumen of the left lower lobe as shown in image A of Figure 1. Bronchoscopy was performed which showed a reddish irregular growth in left main bronchus which bled on touching the probe. The patient had pleural effusion. Pleural fluid cytology was not significant. Biopsy reported as non-small cell lung cancer. CT of whole abdomen was done which had no significant abnormality. PET-CT showed soft tissue lesion in left hilar region causing compression of left lower lobe bronchus with segmental collapse of left lower lobe region measuring 18x17mm consistent with primary malignant lesion. There was presence of metabolically active enlarged mediastinal lymphadenopathy. A decision was made to proceed with surgery. The patient underwent left pneumonectomy with excision of hilar lymph nodes. Gross of the lung specimen showed a growth near the hilus measuring 2 cm cut surface of which was grey white. Rest of the lung showed dilated tiny bronchioles filled with granular material. Histopathology showed sheets of cell showing epidermoid differentiation admixed with mucocytes containing intracellular and extracellular mucin as shown in image B of Figure 1. The solid

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component was composed of large polygonal squamoid cells with pale eosinophilic cytoplasm, moderate nuclear pleomorphism and hyperchromasia with interspersed cystic spaces containing mucin and group of clear cells interspersed within the tumour nest making the diagnosis of High Grade Mucoepidermoid carcinoma (salivary gland type). Lymphovascular and perineural invasion was seen. Tumour was infiltrating adjacent lung parenchyma

and bronchi. None of the lymph nodes showed any evidence of metastasis. The diagnosis was made sure by performing mucicarmine which was positive in cystic spaces surrounded by tumour cells as shown in image C of Figure 1. The tumour cells showed cytoplasmic positivity for mucicarmine. On performing immunohistochemistry EGFR was positive as shown in image D of Figure 1.

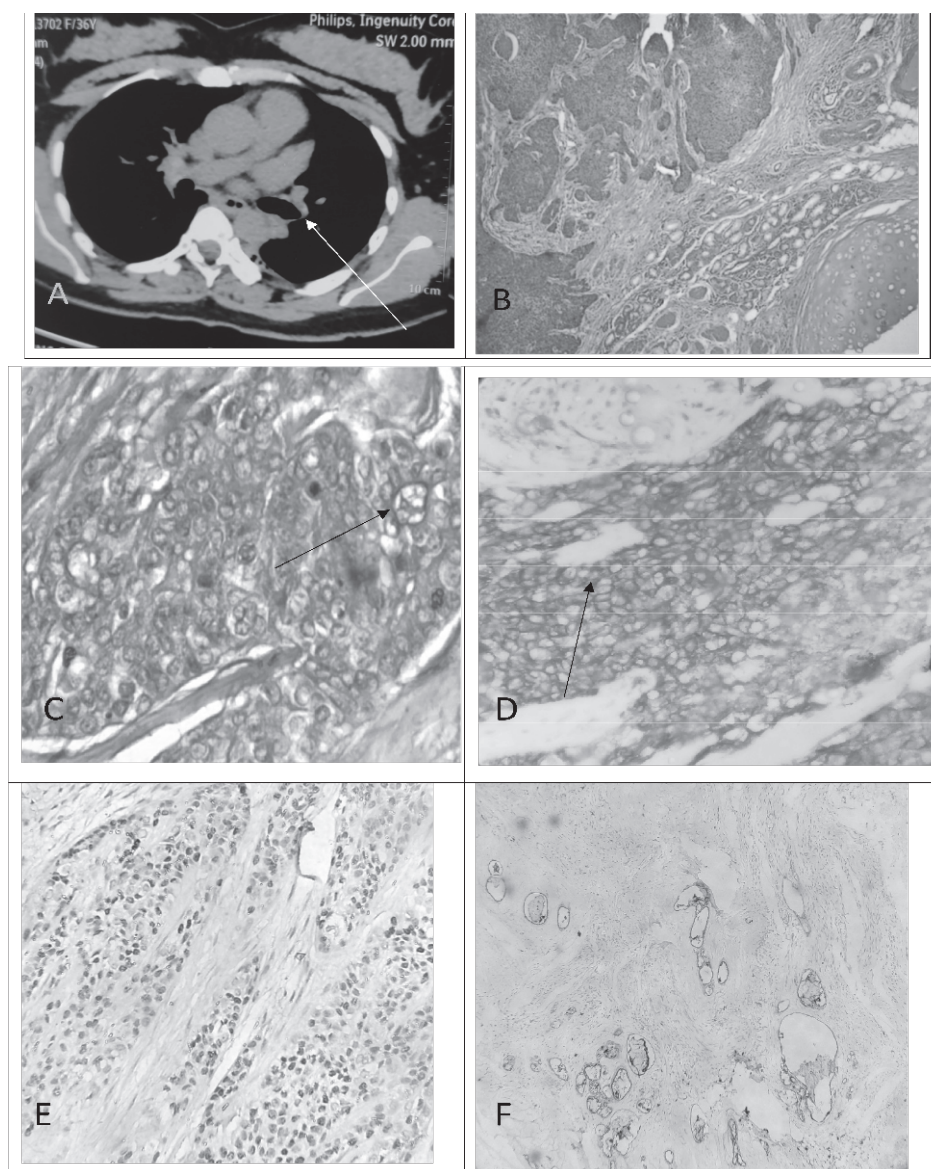


Figure 1: Showing radiological and histopathological images (A) Chest CT of the patient showing patch of mass like consolidation with abrupt cut-off of left lower segmental bronchus (B) Mucoepidermoid carcinoma of lung showing squamous, glandular and cartilaginous component - H &E(100X). (C)Cytoplasm of tumour cells showing positivity for mucicarmine- Mucicarmine stain (400X).(D)IHC staining (400X) membranous positivity of EGFR demonstrated in tumour cells.(E) IHC staining (400X) Nuclear positivity of p63 in the squamous component (F) IHC staining (100X) MUC1 positivity in the glands.

DISCUSSION

Mucoepidermoid carcinoma of the lung is exceedingly rare accounting for 0.1 to 0.5 % of all lung cancers. These tumours may arise from minor salivary glands of tracheobronchial tree presenting as exophytic intraluminal mass on gross and CT, most commonly involving the trachea and /or bronchus. Bronchi show dilatation and are usually filled with mucoid material. Bronchoscopic biopsy and staging plays an important role in diagnosis.

Histologically MEC is comprised of a mixture of cell types including mucin secreting glandular cells, squamous cells, and intermediate cells. The WHO has sub classified MEC into low grade and high grade based on features like cytological atypia, mitotic activity and cellular necrosis. Low grade tumours are composed of three cell types – mucin secreting, squamous and intermediate cells and often show cystic patterns with solid areas. Tumour is land contains both cystic and solid patterns. Cystic components consist of columnar cells with mucin and rare mitosis³.

High grade mucoepidermoid carcinoma is mainly composed of atypical squamoid and intermediate cells, with frequent mitosis and necrosis accompanied by variable number of mucin secreting cells. Immunohistochemically the tumour cells show positive immunostaining for p63 as shown in image E, MUC1 as shown in image F, p40, pan-cytokeratin, CK7 whereas negative for TTF-1, CK20³. Our case was also a high grade MEC with presence of lymphovascular and perineural invasion.

Although metastasis is uncommon it can occur and most commonly seen in regional lymph nodes or other areas of lung tissue⁵. No metastasis was seen in the lymph nodes in our case. Surgical resection remains the standard therapy for patients with pulmonary MEC. Patients with low grade MEC usually have a better prognosis with five-year survival rate approaching 95% but high grade MEC carry a much poorer prognosis.

EGFR may be over expressed in MEC's of salivary gland origin as seen in our case. Gene rearrangements have been discovered in pulmonary MECs like t (11;19) translocation with an associated novel fusion oncogene (CRCT1-MAML2). The role of targeted therapy against EGFR or CRCT1-MAML2 fusion protein is yet to be determined.³

PURPOSE OF THE STUDY

MEC of lung is a rare malignancy. When a young patient even without history of smoking presents with clinical features and radiological evidence of mass lesion in the lung, the diagnosis of MEC should be made after carefully examining different sections of the tumour. These tumours behave less aggressively than squamous cell carcinoma arising from bronchial epithelium. Our case was diagnosed as high-grade squamous cell carcinoma on biopsy and on pneumonectomy it was confirmed as MEC.

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CASE REPORT

Carotid–Jugular Arteriovenous Fistula—A Rare Complication of Central Venous Cannulation: Early Diagnosis And Management Can Prevent Further Complications

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ABSTRACT

Iatrogenic carotid jugular arteriovenous fistula formation after failed attempt to access internal jugular vein for haemodialysis catheter placement is a known but rare complication. If, not diagnosed and treated timely can lead to dreadful consequences like high output heart failure and systemic embolization.

Keywords- Arteriovenous Fistula, Carotid-Jugular Fistula, Central Venous Cannulation, Haemodialysis Catheter.

INTRODUCTION

Double lumen catheters are commonly used as temporary vascular access in patients requiring acute haemodialysis (HD). Internal jugular vein (IJV), considering its relative lesser complication rates as compared to subclavian or femoral cannulation, has become the preferred site for temporary haemodialysis catheter placement¹. Arterial puncture is a known complication of IJV cannulation with an incidence of 29.9%^{2,3} which can lead to life threatening bleeding, hematoma formation, pseudo aneurysm, stroke due to thromboembolism and arterio-venous fistula (AVF) formation. Formation of fistula between carotid artery and internal jugular vein after internal jugular vein cannulation is a rare complication with probably only one case reported in India⁴. Central venous cannulation has been carried out traditionally using the landmark technique. Use of ultrasound is advisable for central venous cannulation, whenever available⁵. In India the landmark technique is still being widely used.

Here, we report a case of acquired carotid- internal jugular arteriovenous fistula after multiple failed attempts to access internal jugular vein as an access for haemodialysis.

CASE HISTORY

A 26 year old female presented to our centre with complains of abnormal sensation in right side of her neck. She also gave history of failed venepuncture in the neck two months back. The patient was asymptomatic two months ago when she developed multiple episodes of loose stools and vomiting. Two days later her urine output decreased and she started having shortness of breath. The patient was then admitted at a hospital and was started on intravenous medication. Over the next 24 hours, she became anuric and her creatinine was found to be 7.1mg/dl. Haemodialysis catheter insertion was attempted at right internal jugular vein, which failed after multiple attempts. The patient was initiated on haemodialysis via the right femoral vein on the next day. She received eight sessions of haemodialysis over the next twenty days. Renal biopsy was done to assess the cause of Acute Kidney Injury, which revealed diffuse renal cortical necrosis of the sampled cortical area. The patient noticed a palpable thrill over the right lateral cervical region. Over the course of the next week, she had a partial renal recovery. Her urine out improved to more than 1500ml/day and she was discharged and referred to our centre for further management.

On clinical evaluation a continuous thrill was palpable at the right cervical region. The patient was normotensive with no other significant findings. Her creatinine was 4.5 mg/dl and urine output was 1600ml/day. Doppler evaluation revealed an abnormal fistulous communication of size 11 x 6 mm between the lower one third of right common carotid artery and lower one third of right internal jugular vein, at the level of lower pole of right thyroid lobe. Origin of the fistulous opening in right common carotid was 16mm distal to the

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bifurcation of the right brachiocephalic artery. The patient was at a high risk for contrast induced nephropathy, so neither angiography nor endovascular repair could be considered. An open surgical repair under general anaesthesia was planned. Anterior cervical thyroid incision was given. Platysma and sternal end of the sternocleidomastoid were cut. The common carotid artery-internal jugular fistula was exposed. The common carotid artery, subclavian artery and internal jugular vein were looped. Fistulous tract was found between common carotid artery and internal jugular vein. The tract was divided, both ends were closed with 6-0 prolene suture. The continuous thrill disappeared. The patient developed accelerated hypertension, in the immediate post-operative period with her blood pressure reaching 240/150mm Hg. She was started on injection nitroglycerine infusion and sublingual nifedipine for blood pressure control. This was tapered over the next 5 days. The patient made a full recovery with no cardiovascular or neurological deficit after 25 days of hospital stay. Post-operative Doppler revealed normal anatomy and flow. Assessment in the nephrology clinic at 6 months after discharge, showed no complication.

DISCUSSION

A carotid-jugular arteriovenous fistula is a direct communication between the carotid artery and the jugular vein. It can be either congenital or acquired. Acquired fistulae are most frequently caused by penetrating trauma or are iatrogenic⁶. Ortiz et al.⁷ in 1976, first reported the arteriovenous fistula from an internal jugular vein catheter placement, a fistula between the inferior thyroid artery and the internal jugular vein.

Clinical features depend on time of presentation, size of fistula and its proximity to heart, left to right shunting of blood and the distensibility of the vessels involved. Carotid artery –internal jugular vein fistula can present as pulsatile neck swelling, presence of distended veins, thrill on palpation, and continuous murmur with systolic accentuation, or it may be incidentally detected on the neck evaluation for a different purpose⁸. AVF results in certain physiological changes such as increased venous return, with simultaneous fall in total peripheral resistance: resulting in immediate rise in heart rate, stroke volume, cardiac output, and cardiac work as a physiologic response to the overload, and the course is towards irreversible high output cardiac failure. Heart failure is a

late presentation of undiagnosed, untreated large AVF (diameter >8mm).

Colour flow Doppler is a sensitive modality for diagnosing AV fistula⁹. Computed Tomography Angiography (CTA) provides the best spatial resolution of catheter angiography and offers the best three-dimensional localization of the AVF within the tissues if surgical repair is planned. Magnetic resonance angiography spatial resolution is good though inferior to CTA. Conventional catheter angiography still being the gold standard⁸.

Untreated fistulae can lead to serious complications including systemic embolization, high output cardiac failure and infections. Though rare, but neurological deficits in the form of visual disturbance, tinnitus, or hemiparesis either from steal phenomenon or from venous congestion in the dural venous sinuses may occur¹⁰.

Timely diagnosis and intervention can prevent these dreadful complications, even in large sized fistulae, as in our case (11mm × 6mm).

Being minimally invasive, endovascular treatment by stent grafts and coils is gaining favour today but, the final approach is to be decided on case to case basis, as was done in our case.

Droll et al¹¹ in 2004 recommended certain measures to prevent inadvertent arterial puncture during internal jugular vein catheterisation such as limiting the head rotation to 40 degrees, using smaller gauge needle as introducer needle and ultrasound guided catheterisation wherever available.

Carotid artery-internal jugular vein arteriovenous fistula, though rare is a dreadful complication of venous puncture for haemodialysis catheter insertion. All precautions should be taken to prevent arterial puncture during IJV cannulation. In such patients, the physician should be vigilant for any sign and symptoms of carotid jugular fistula and prompt correction should be considered. Use of ultrasound is recommended for central venous access to prevent inadvertent arterial injuries.

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CASE REPORT

Intramuscular Massetric Hemangioma Resembling Parotid Swelling - A Rare Case Report

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ABSTRACT

Intramuscular hemangiomas (IMHs) are very rare and constitute approximately 1% of all hemangiomas. 0.8% of all hemangiomas and 10–20% of all intramuscular hemangiomas are located in the head and neck muscles, arising most frequently from the masseter and trapezius muscles. Due to its location it is often mistaken for a parotid swelling and rarely is an accurate pre-operative diagnosis achieved clinically. Currently, MRI is the standard imaging technique for diagnosing soft-tissue hemangioma.

The optimal management is surgical resection. Here is the case of 16 year old male patient presented with right side cheek swelling since three years. Presumptive diagnosis of massetric intramuscular hemangioma was made on the basis of CT and MRI findings. Surgical resection was done and histopathological findings confirmed the diagnosis. Intramuscular hemangiomas are rare in the head and neck region, and it should be considered in the differential diagnosis of masses in these regions. The knowledge of the nature and recurrence rate of an intramuscular hemangioma is useful for appropriate management.

Keywords-Intramuscular massetric hemangioma; rare case; MRI

INTRODUCTION

A hemangioma is a benign vascular tumor derived from blood vessel cell types. Intramuscular hemangiomas (IMHs) are very rare and constitute approximately 1% of all hemangiomas¹. They occur most frequently in the large muscles of the upper and lower extremities and trunk². 0.8% of all hemangiomas and 10–20% of all intramuscular hemangiomas are located in the head and neck muscles, arising most frequently from the masseter

and trapezius muscles³. Intramuscular hemangiomas [IMH] generally occur in the first three decades of life⁴. Although intramuscular hemangiomas have shown an equal sex distribution, involvement of the masseter has a definite male predominance⁵.

Intramuscular hemangiomas generally present as progressively enlarging and often painful lesions. Thrills, bruits, compressibility, and pulsation are usually absent⁶⁻⁸. Preoperative diagnosis of IMH of the masseter muscle is problematic because they may be confused with parotid tumor or other muscular lesions. In a patient with a soft-tissue mass suspected of to be a hemangioma, MRIs may provide more specific information regarding the characteristics, origin, and extent of the lesion⁹.

CASE REPORT

A 16 year old male presented to ENT department with chief complaint of right side cheek swelling since three years. Patient had significant past history of trauma at the same at six months of age.

The swelling was firm, oval situated over right side parotid region measuring approximately 3x4cm and was non-pulsatile, non-transilluminant and non-compressible. No audible bruit and thrill was present. Facial movements, intraoral examinations and overlying skin were normal. Patient had undergone biopsy of the same 3 months back at other institute which revealed chronic parotitis on histology.

Fine needle aspiration cytology and ultrasound examination were inconclusive.

The contrast enhanced computerized tomography was done to know the relationship of lesion with respect to bony landmarks which showed a well-defined heterogeneous mass lesion involving the right masseter muscle which was highly vascular.[Figure 1]

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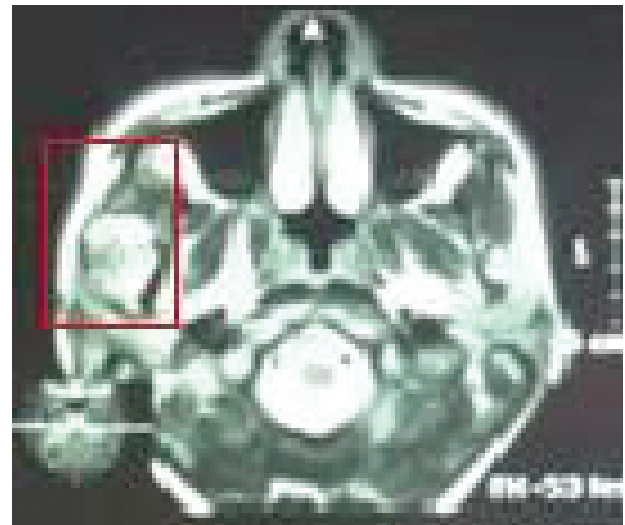
Figure 1: Contrast enhanced computerized tomography showing well defined heterogeneous mass lesion involving the right masseter muscle which was highly vascular (red marked area)

Gadolinium enhanced MRI revealed a well-defined, well-margined mildly enhancing mass lesion of size 33*23 mm, slightly hyperintense to the masseter muscle and hypointense to the parotid gland on T1-weighted images [Figure 2 (a)], markedly hyperintense to both the masseter muscle and parotid gland on T2-weighted images [Figure 2 (b)].

These findings were highly suggestive of the intramuscular hemangioma of the masseter muscle.



(a)

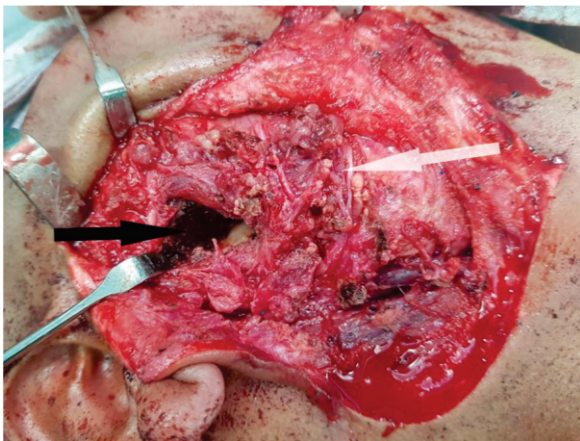


(b)

Figure 2 : (a) Gadolinium enhanced MRI revealed a well - defined, well -marginated mildly enhancing mass lesion slightly hyperintense to the masseter muscle and hypointense to the parotid gland on T1-weighted image. (b) Gadolinium enhanced MRI revealed a well - defined, well - marginated mildly enhancing mass lesion markedly hyperintense to both the masseter muscle and parotid gland on T2-weighted image

Transparotid excision of swelling was planned. Modified Blair's incision was given including the old incision, fibrosis was found of previous biopsy, the superficial parotidectomy was done to identify facial nerve trunk and its all terminal branches. The facial nerve fibres lying over massetric bed [Figure 3], were separated from masseter and gently uplifted with hook and the lesion was approached between the zygomatic and temporal branches. Dissection was done through massetric muscle to expose the lesion. Then with harmonic scalpel the tumor was removed en-toto [Figure 4]. Post-surgically, the patient had grade 3 facial weakness which improved to grade 1 over 3 weeks.

Histopathology revealed that the given soft tissue section showed skeletal muscle infiltrated by fibrovascular connective tissue exhibiting numerous large dilated thin walled as well as smaller thick walled vascular spaces filled with RBCs. There was also proliferation of small and capillary sized of blood vessels in between. These blood vessels were lined by the single layer of endothelial cells. There was no evidence of malignancy. These findings suggested intramuscular mixed hemangioma [Figure 5]



**Figure 3: (White arrow –branches of facial nerve)
(Black arrow- area from where hemangioma was excised within massetric muscle)**

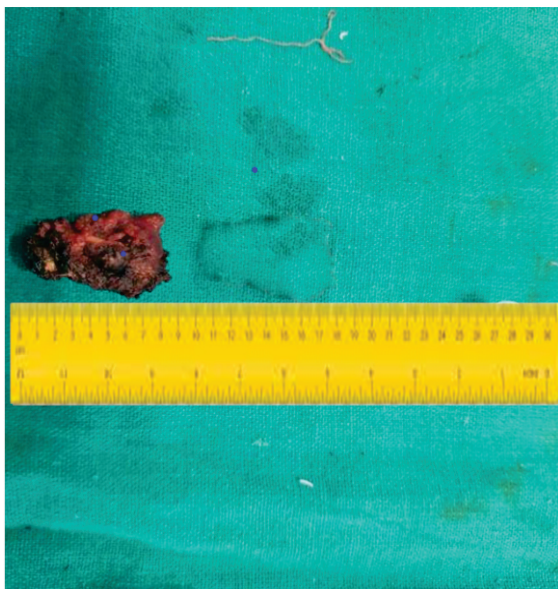


Figure 4 : excised specimen

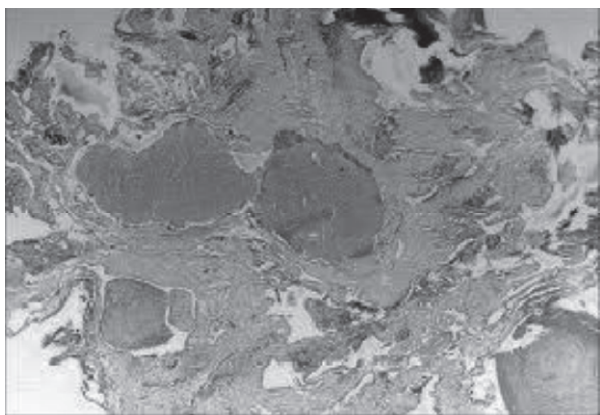


Figure 5: Microscopic examination - Numerous dilated blood vessels containing blood with some small capillary-sized blood vessel

DISCUSSION

Vascular lesions involving the skeletal musculature are uncommon tumors characterized by the proliferation of blood vessels, occurring most frequently in the large muscles of the upper and lower extremities and trunk², first described by Liston¹⁰. Numerous classifications of vascular lesions exist in the English literature. Mulliken and Glowacki classified vascular lesions as vascular malformations and hemangiomas, based on their clinical appearance, histopathologic features and biologic behavior¹¹. Allen & Enzinger¹² classified them histologically as (1) capillary (vessels smaller than 140 micrometer in diameter), (2) cavernous (vessels larger than 140 micrometer in diameter) or (3) mixed (consisting of both small and large vessels). In our case, the tumor can be classified as hemangioma of mixed type. Etiopathogenesis remains unclear although various theories have been proposed to explain its etiology. The most likely explanation is that the intramuscular hemangioma is a congenital mass, arising by abnormal embryonic sequestrations, similar to congenital arteriovenous malformations¹³. Traumatic etiologies have also been suggested¹⁴. We feel that the most probable cause in our case could be direct trauma to the cheek in childhood. As in intramuscular hemangiomas the classical sings of thrills, bruits, compressibility, and pulsation are usually absent so these tumors can be confused clinically with a large number of entities like salivary neoplasm's, cysts, lymphangiomas, rhabdomyosarcomas, masseteric hypertrophy, and schwannomas¹². Diagnosis of such vascular lesions is often challenging. FNAC is inconclusive in arriving at a diagnosis as it yields only a bloody aspirate⁴. Superselective arteriography with subtraction clearly defines the altered vascular pattern and flow dynamics including feeder vessels and also opens up therapeutic modalities. However it may fail to demonstrate low flow lesions adding to the diagnostic difficulty. Though contrast CT may demonstrate the vascular nature of the tumor MRI has shown superiority in the exquisite delineation and contrast of the lesion from its surroundings due to its multiplanar capability. As in our case, MRI findings were identical with the literature and our case had characteristic sign for hemangioma- like high signal intensity on T2-weighted MRI images, with marked enhancement after gadolinium administration. Management of intramuscular haemangioma should be

individualized according to the tumor location and extent, tumor growth rate, anatomical accessibility, patient age and cosmetic considerations¹⁵. Many treatment modalities like cryotherapy, radiation therapy, steroid administration, embolization, sclerosing agents, carbon dioxide snow and blood vessel ligation have been advocated¹⁶. But the treatment of choice at present remains surgical excision, the indications for surgery being symptomatic but stable tumors, sudden rapid acceleration of tumor growth, gross functional impairment, local skin necrosis, thrombocytopenia, cosmetic deformity and suspicious of malignancy¹⁷. In this case we choose surgery as treatment of choice because the tumor was growing in size and causing disfigurement of the face. Local recurrences occur in approximately 18% due to incomplete surgical resection¹⁶. Spontaneous regression does not occur. Regional and distant metastasis has not been reported. In this case also, no recurrence has been noted upto 1 year of follow up.

CONCLUSION

Intramuscular hemangiomas are rare in the head and neck region, and it should be considered in the differential diagnosis of masses in these regions. Its diagnosis is difficult because of its rarity and non-specific signs. The knowledge of the nature and recurrence rate of an intramuscular hemangioma is useful for appropriate management.

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